Valoración de los Últimos Resultados CVCs en Relación con el Control de la Diabetes

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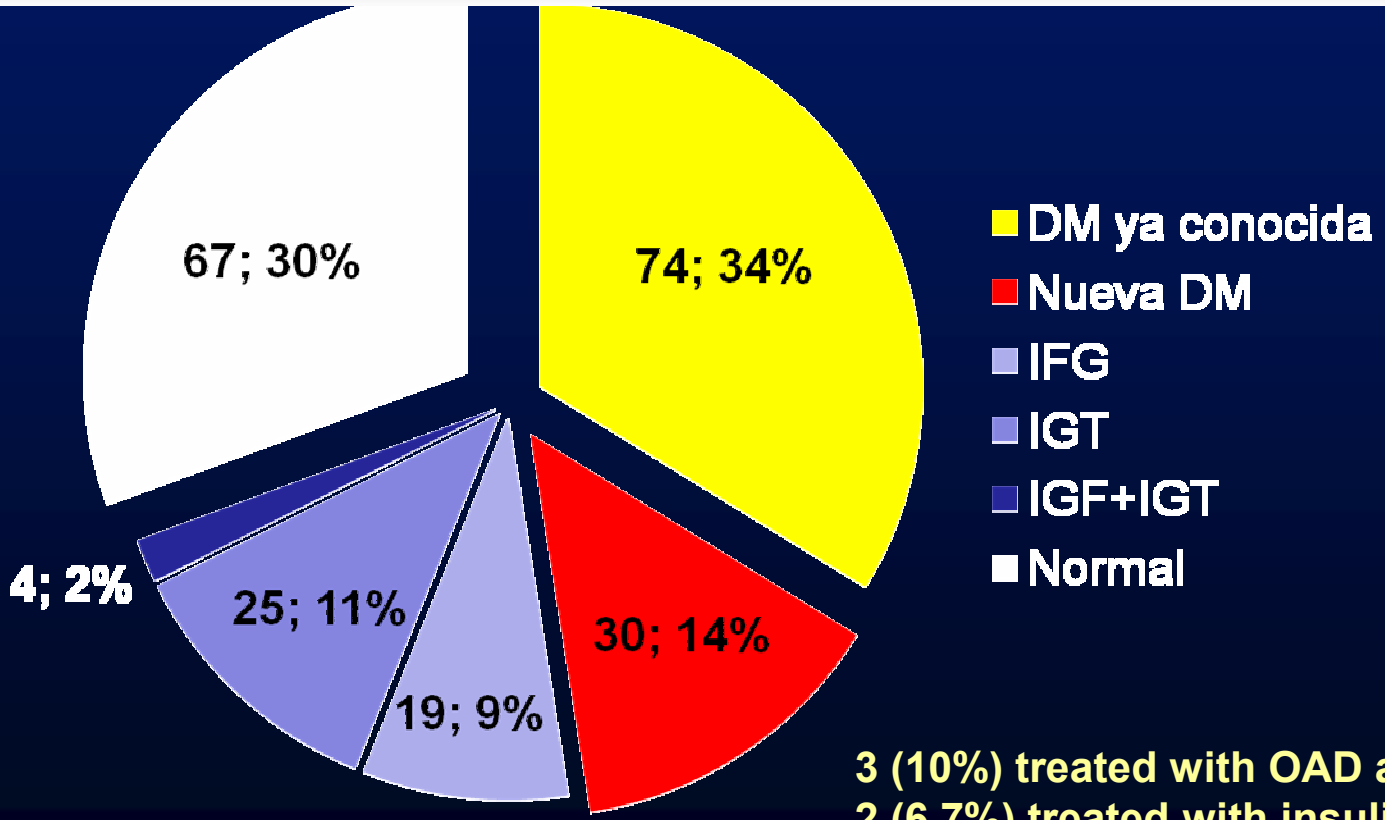
Control Glucémico en la Cardiopatía Isquémica

- **Diabetes y Cardiopatía Isquémica**
- Control Glucémico en Diabéticos con CI
- Fármacos antidiabéticos en Pacientes con CI
- Prevención integral

ACUTE CORONARY SYNDROME AND DIABETES

RESULTADOS GLOBALES

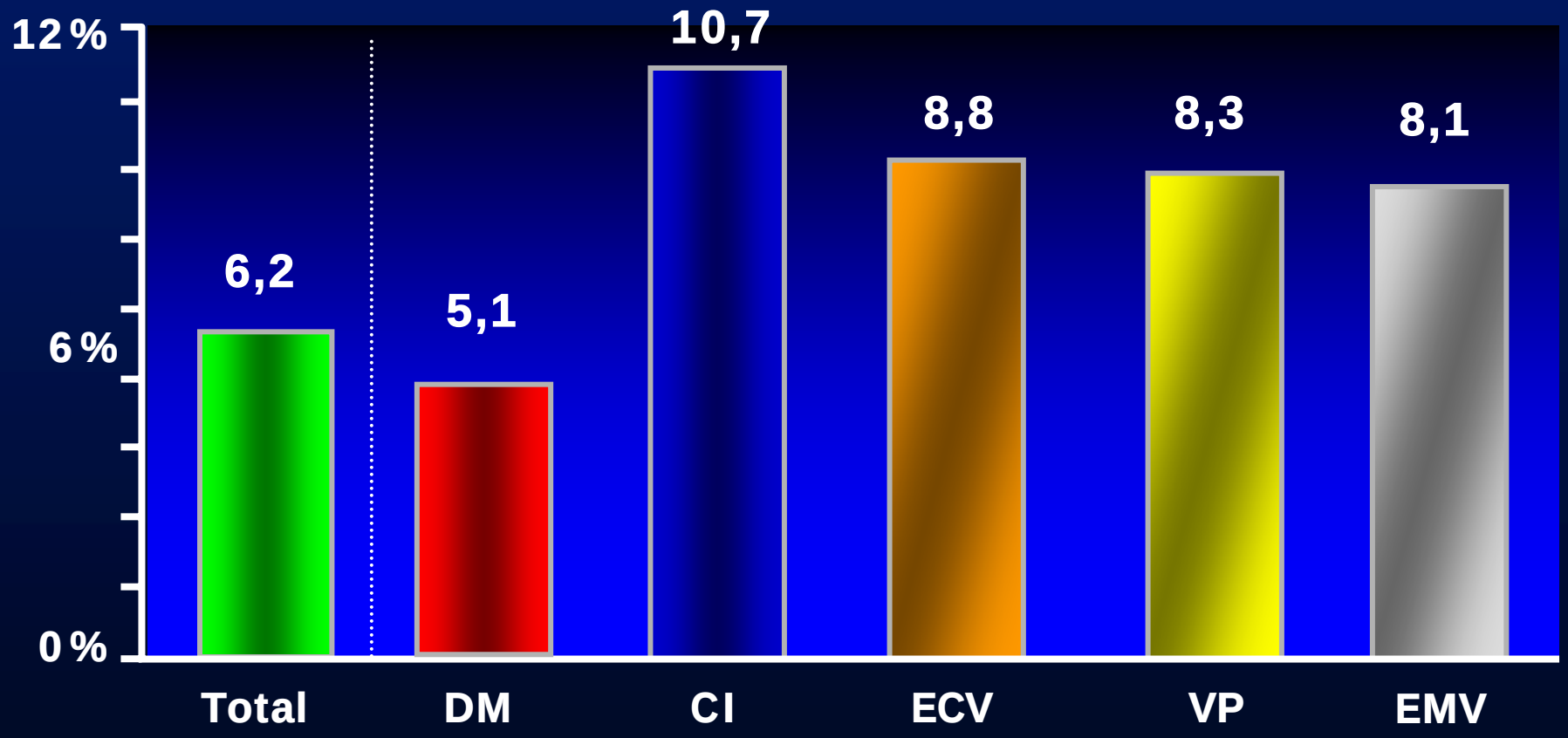
219 patients



3 (10%) treated with OAD at discharge
2 (6,7%) treated with insulin at discharge

Estudio DM-Barbanza

MORTALIDAD BRUTA

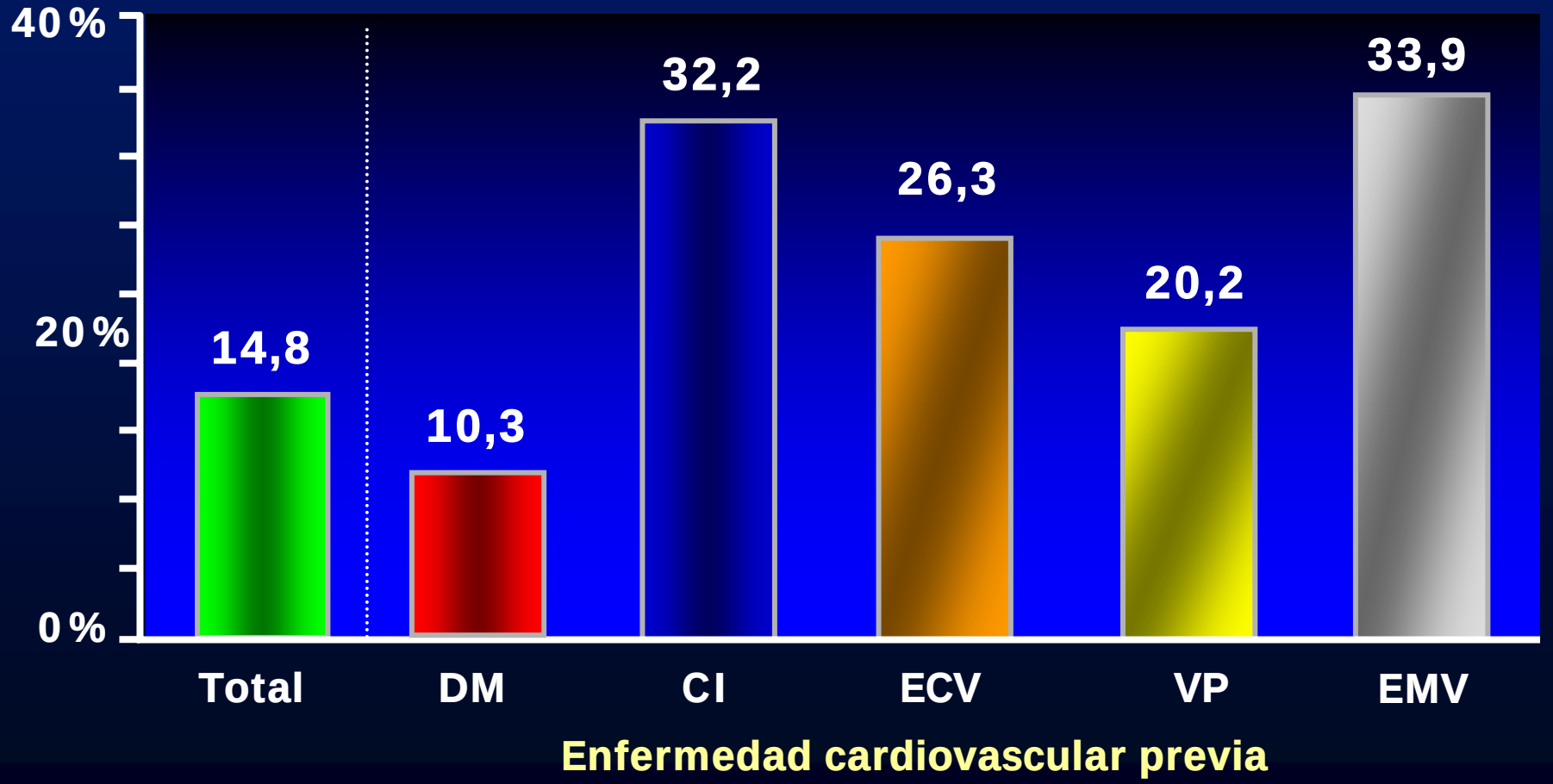


Seguimiento medio: 44,6 meses
109 pacientes perdidos

González-Juanatey JR et al (Grupo BARBANZA). Rev Esp Cardiol 2008

Estudio DM-Barbanza

EXITUS Y/O INGRESO CV



Seguimiento medio: 44,6 meses

109 pacientes perdidos

González-Juanatey JR et al (Grupo BARBANZA). Rev Esp Cardiol 2008

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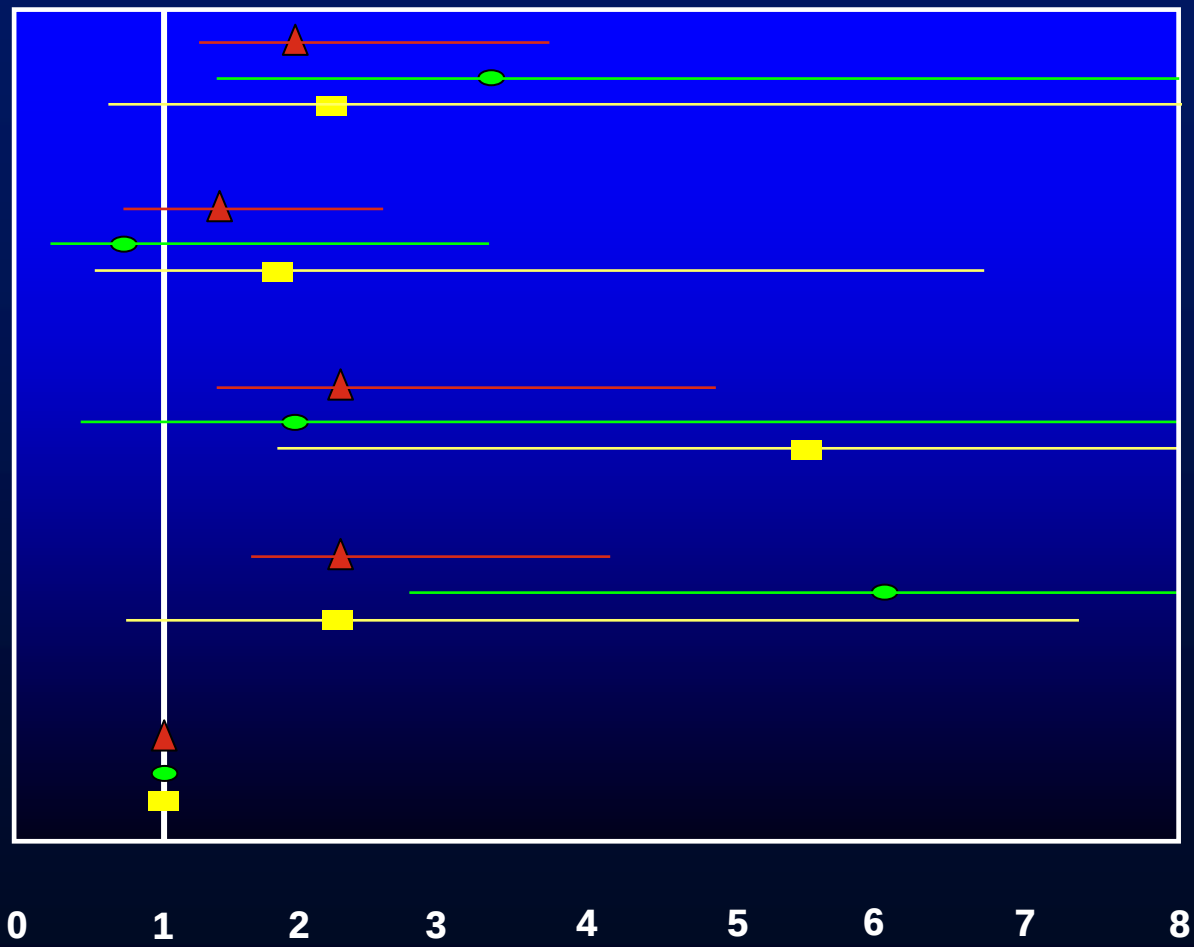
Riesgo de eventos y mortalidad



	OR	(IC-95%)
EMV	2,12	(1,17-3,83)
	3,53	(1,35-9,19)
	2,43	(0,66-8,89)
VP	1,46	(0,81-2,60)
	0,76	(0,18-3,29)
	1,84	(0,51-6,61)
ECV	2,51	(1,28-4,92)
	1,97	(0,45-8,67)
	5,58	(1,88-16-53)
CI	2,48	(1,51-4,07)
	6,01	(2,92-7,45)
	2,45	(0,80-7,45)

González-Juanatey JR et al (Grupo BARBANZA). Rev Esp Cardiol 2008

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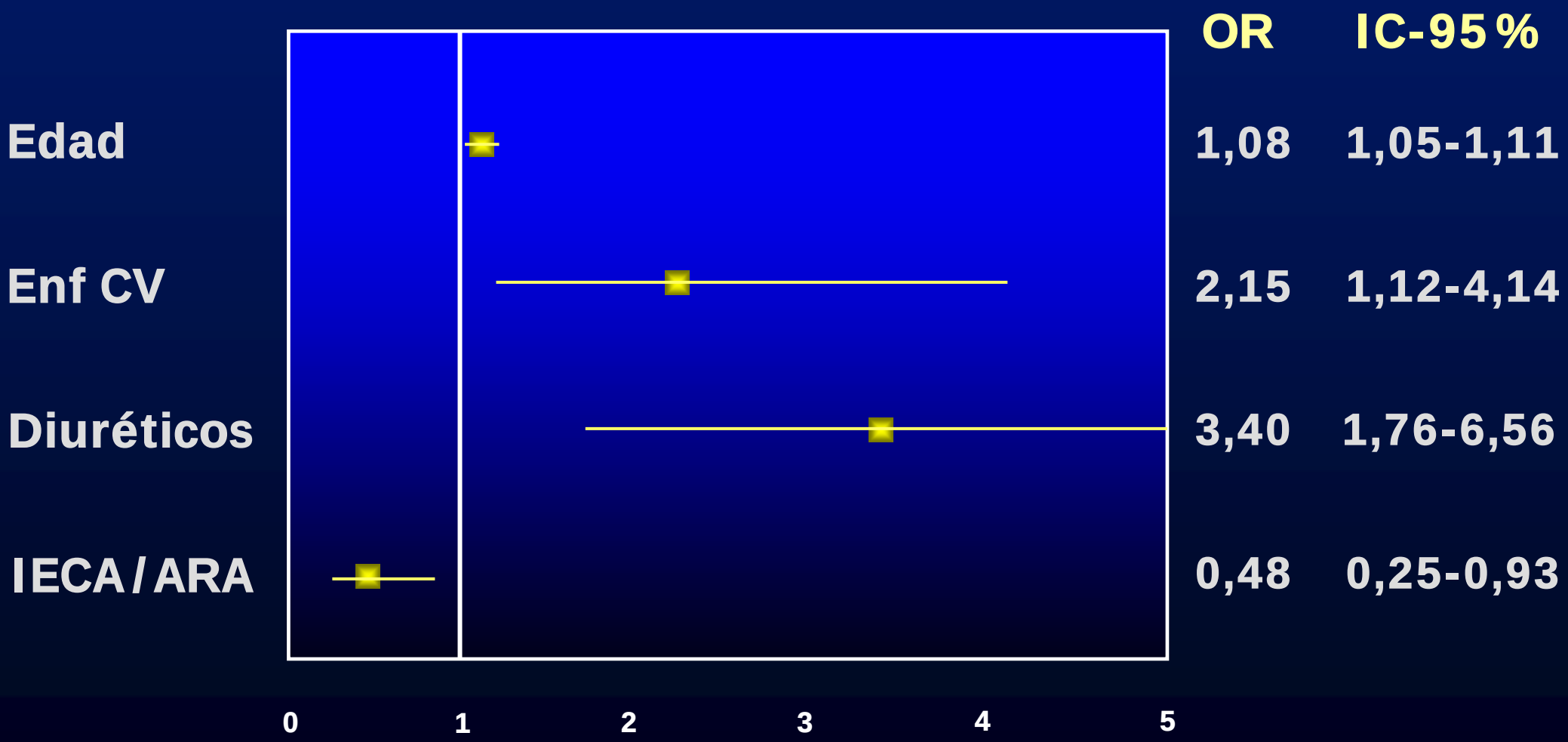
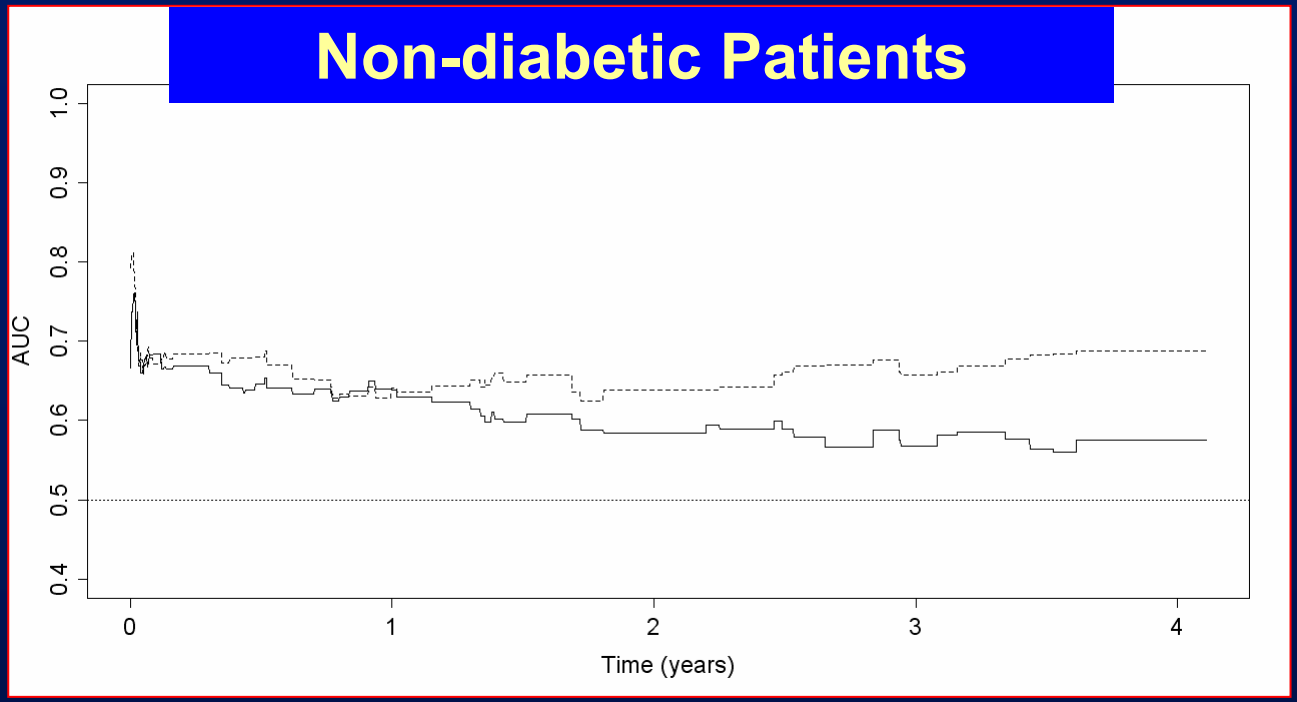
Determinantes de mortalidad



González-Juanatey JR et al (Grupo BARBANZA). Rev Esp Cardiol 2008

Glucose and Mortality in ACS Patients

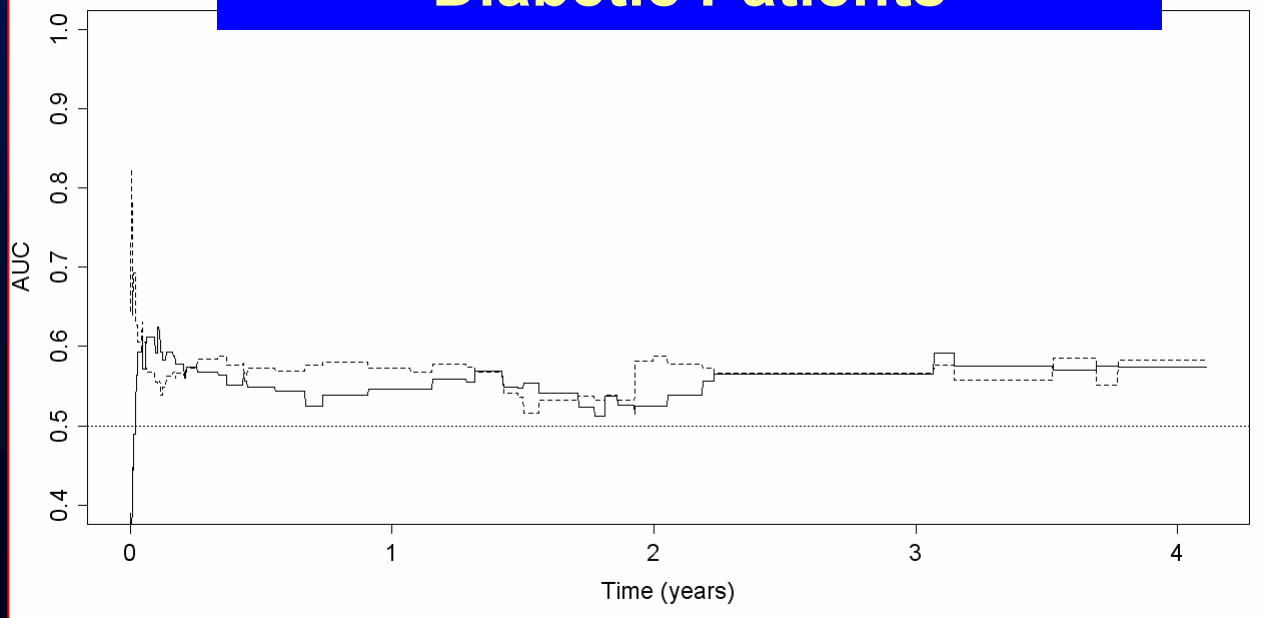
Non-diabetic Patients



Fasting glucose: dotted lines

Admission glucose: solid lines

Diabetic Patients



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Glucose and Mortality in ACS Patients

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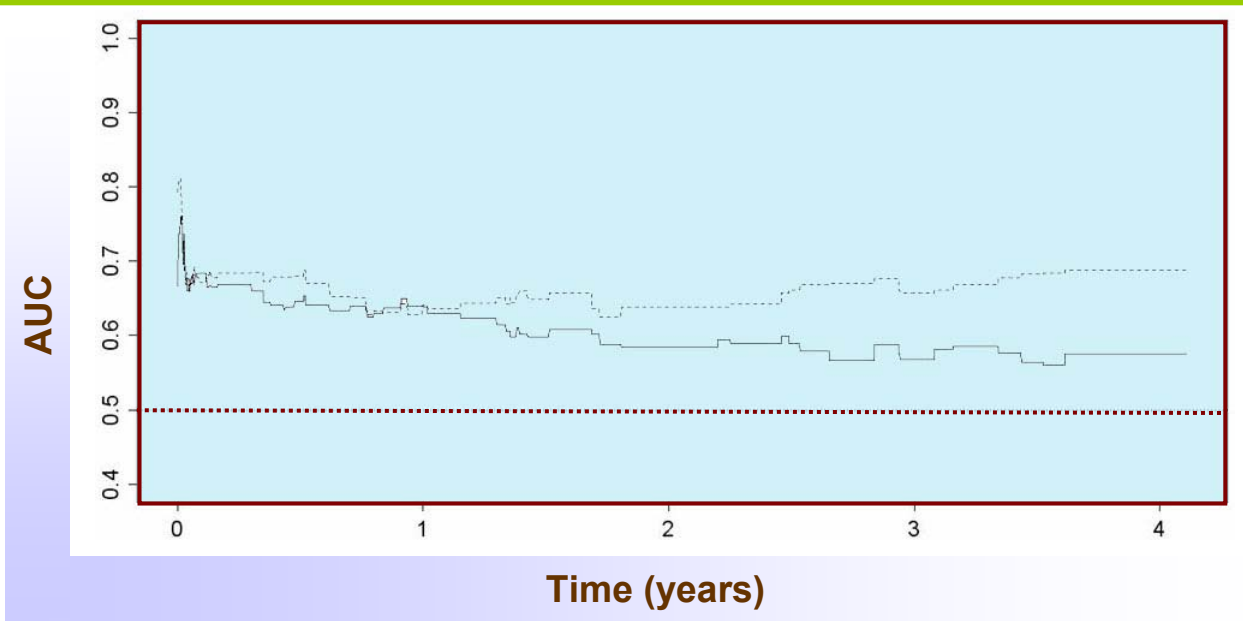
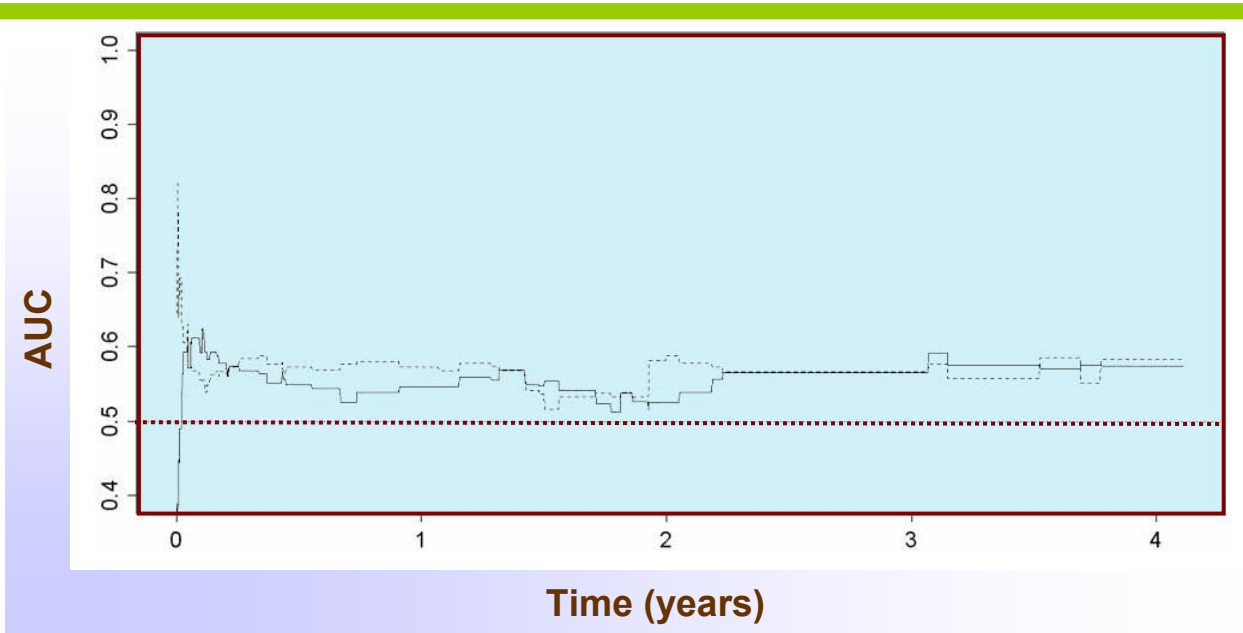


Diabetic Patients

Fasting glucose: dotted lines

Admission glucose: solid lines



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Objetivos Glicémicos para el Cuidado de Pacientes con Diabetes Recomendados por Varias Organizaciones

Organización	HbA_{1c} (%)	FPG (mmol/L)	PG post-prandial (mmol/L)
ADA	< 7	≤ 6,7 (120)	Nada
IDF-Europa	≤ 6,5	≤ 6,0 (108)	≤ 7,5 (135)
AACE	≤ 6,5	≤6,0 (108)	≤ 7,8 (140)

ESC/EASD Eur Heart J 2007;28:88-136

STATEMENT OF ADA, ACC y AHA (ADVANCE, ACCORD, VADT)

- **Microvacular Dis.**: HbA1c < 7 % (ACC/AHA 1 A)
- **Macrovascular Dis:** HbA1c < 7 % (ACC/AHA IIb A)
  - Individualization:
  - **"Lowering A1c to below 7 %"** in pactients without risk of hypoglycemia, patients with short duration of diabetes, long life expectancy, and no significant cardiovascular disease. (ACC/AHA IIa C)
  - **"Less stringent A1c goal"** for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, comorbid conditions, long-standing diabetes. (ACC/AHA IIa C)

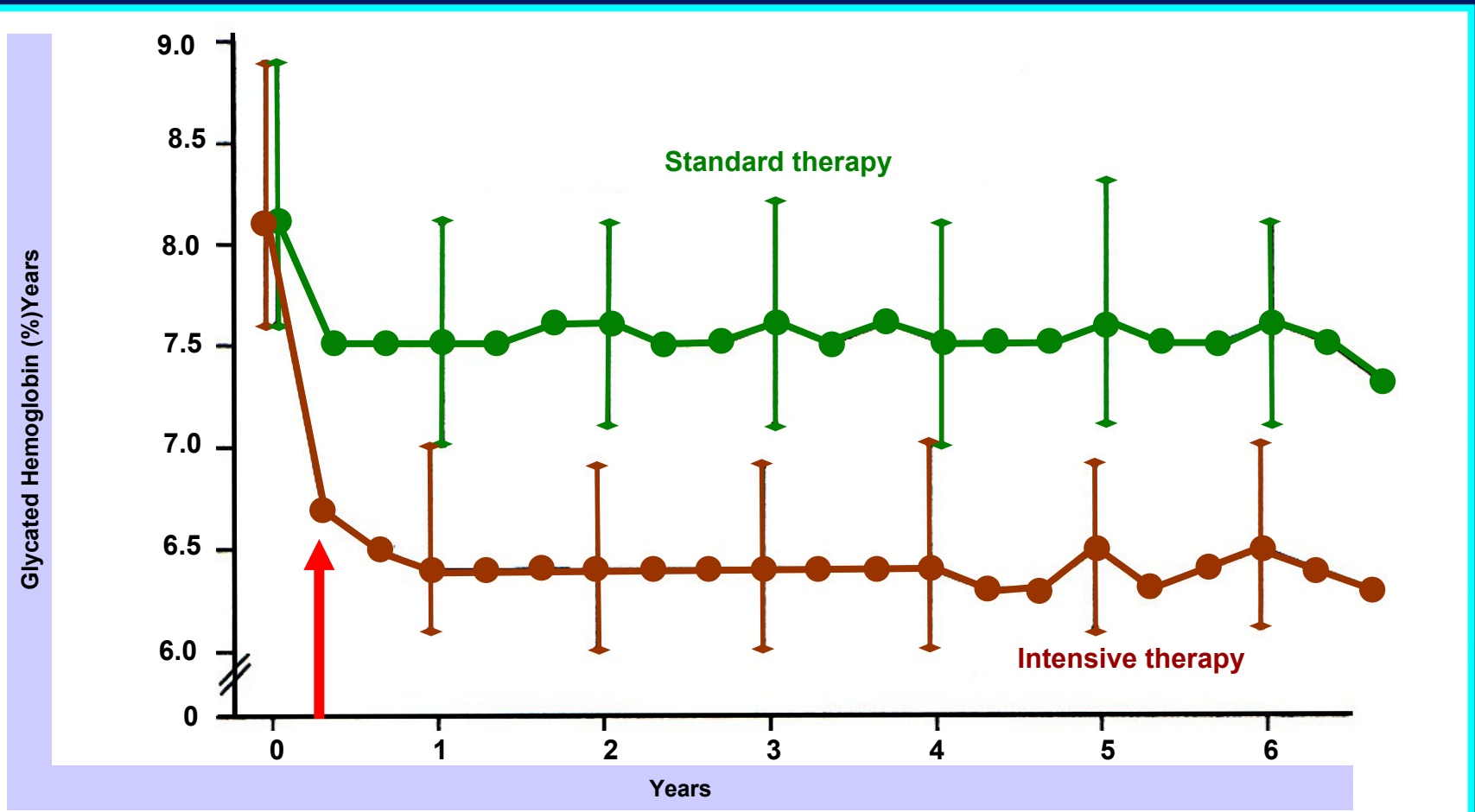
Circulation 2009; 119: 0-0

Objetivos de Tratamiento en Pacientes con Diabetes Tipo 2. Guias Europeas Prevención-07

	Unidad	Objetivo
HbA1C (DCCT)	HbA_{1C} (%)	≤ **6,5 si es posible**
Glucosa en plasma	ayunas/preprandial mmol/L (mg/dL)	**<6,0 (110) si es posible**
	postprandial mmol/L (mg/dL)	**< 7,5 (135) si es posible**
Presión arterial	mmHg	≤ **130/80**
Colesterol total	mmol/L (mg/dL) mmol/L (mg/dL)	**< 4,5 (175)** **< 4,0 (155) si es posible**
Colesterol LDL	mmol/L (mg/dL) mmol/L (mg/dL)	**< 2,5 (100)** **< 2,0 (80) si es posible**

Effects of Intensive Glucose Lowering in Type 2 Diabetes

Median Glycated Hemoglobin Levels at Each Study Visit



No. at Risk							
Standard	5019	4774	4588	3186	1744	455	436
Intensive	5119	4768	4585	3165	1706	476	471

I bars denote interquartile ranges

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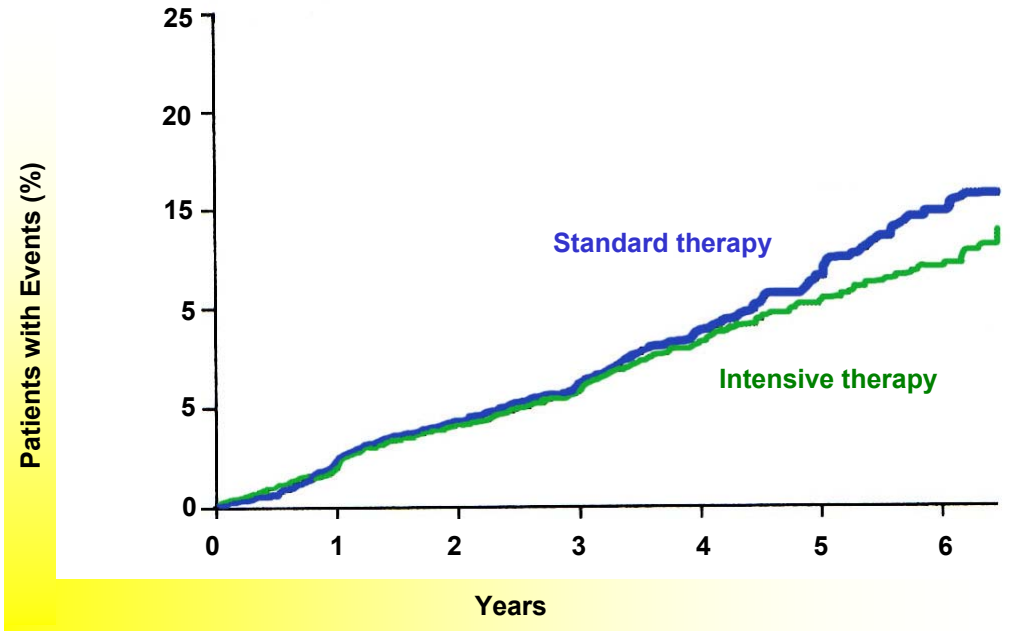
The Action to Control Cardiovascular Risk in Diabetes Study Group. N Engl J Med 2008;358:2545-59

Effects of Intensive Glucose Lowering in Type 2 Diabetes

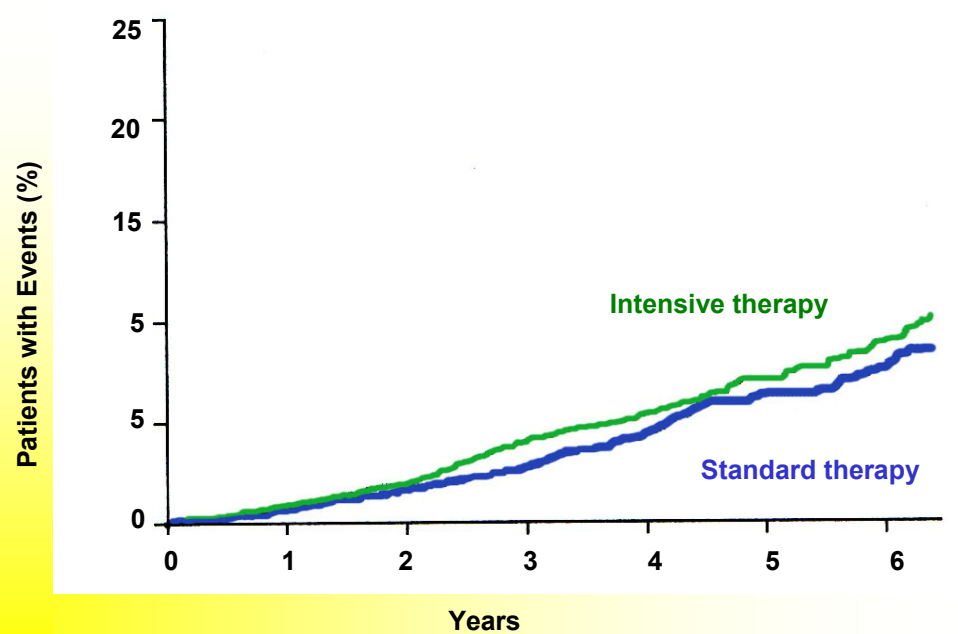
Kaplan-Meier Curves for the Primary Outcome and Death from Any Cause

Primary Outcome



No. at Risk							
Intensive therapy	5128	4843	4390	2839	1337	475	448
Standard therapy	5123	4827	4262	2702	1186	440	395

Death from Any cause



No. at Risk							
Intensive therapy	5128	4972	48803	3250	17484	523	506
Standard therapy	5123	4971	4700	3180	1642	499	480

The Action to Control Cardiovascular Risk in Diabetes Study Group. N Engl J Med 2008;358:2545-59

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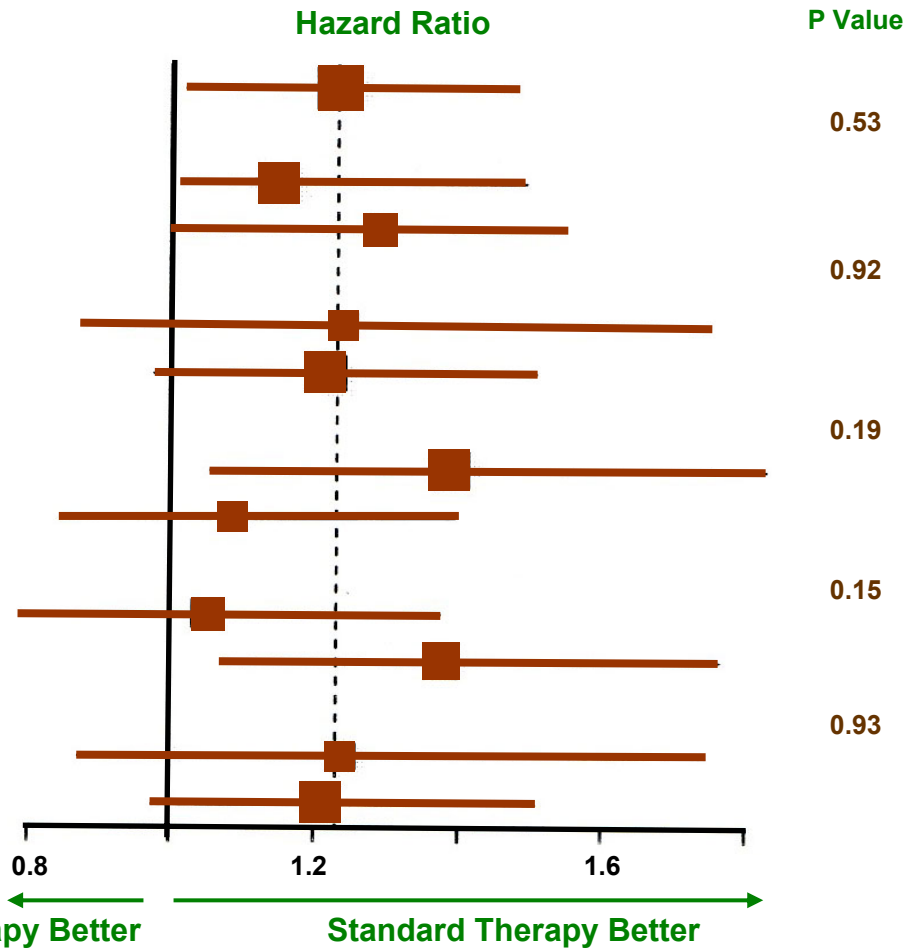
Effects of Intensive Glucose Lowering in Type 2 Diabetes

Hazard Ratios for the Primary Outcome and Death from Any Cause in Prespecified Subgroups

Subgroup	No. of Patients	No. of Events	P Value
Total	10,251	723	
Previous cardiovascular event			
No	6,643	330	0.53
Yes	3,608	393	
Sex			
Female	3,952	212	0.92
Male	6,299	511	
Age at baseline			
<65 yr	6,779	383	0.19
≥65 yr	3,472	340	
Glycated hemoglobin at baseline			
≤8.0%	4,868	284	0.15
>8.0%	5,360	438	
Race			
Nonwhite	3,647	222	0.93
White	6,604	501	

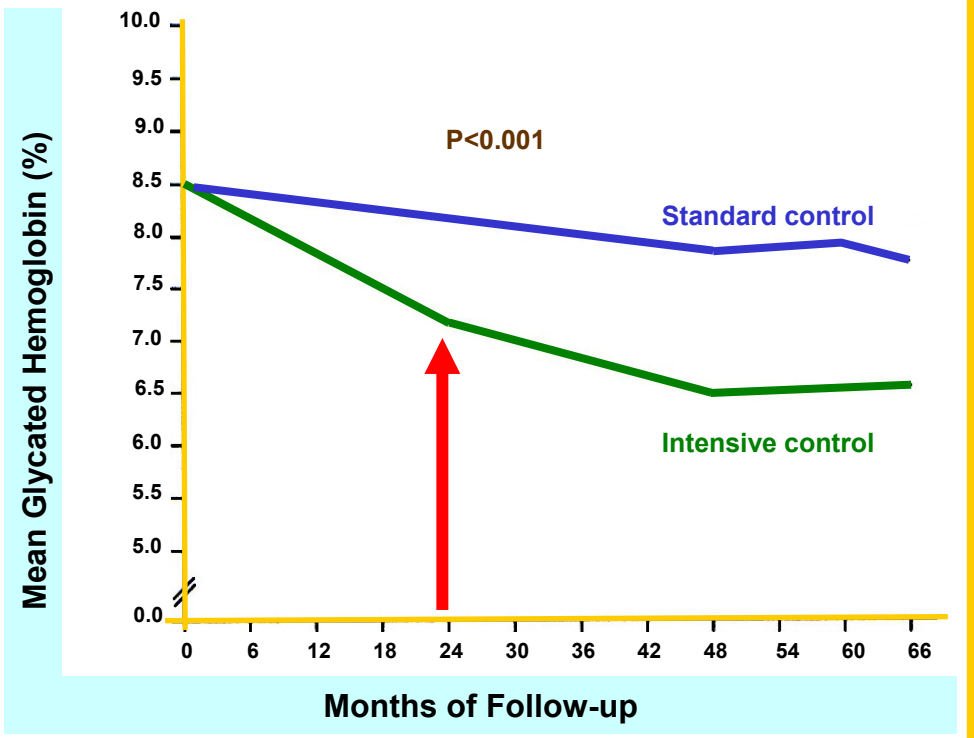


Data regarding glycated haemoglobin levels and baseline are presented for 10,288 patients because a baseline level was not available for 23 patients. Horizontal bars represent the 95% confidence interval, and vertical dashed lines indicate the overall hazard ratio. The sine of each square is proportional to the number of patients

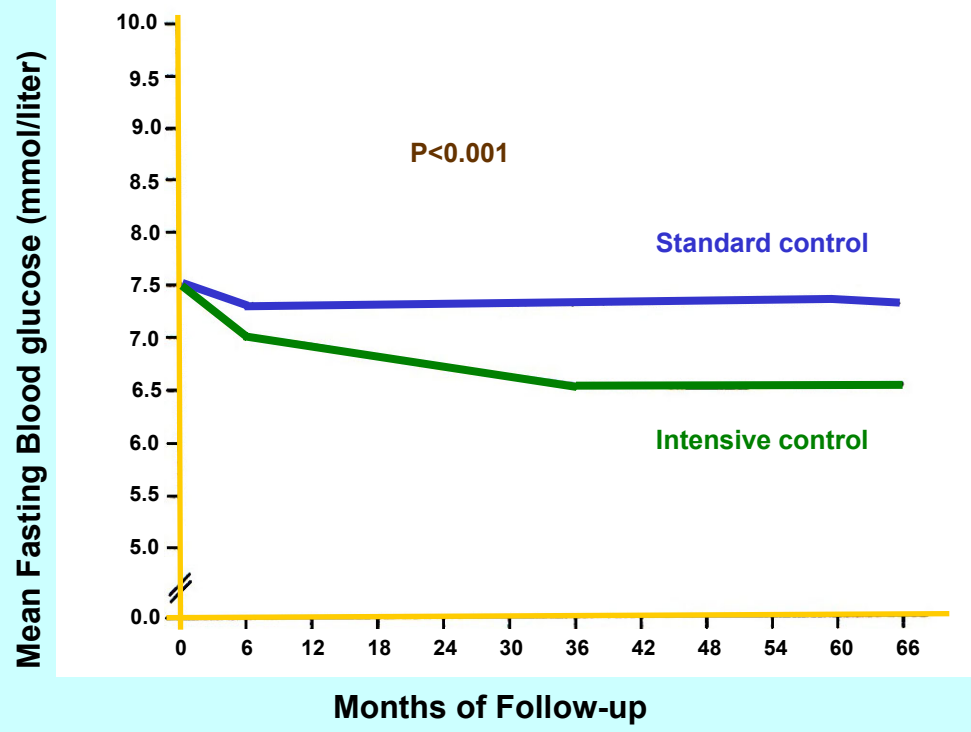
The Action to Control Cardiovascular Risk in Diabetes Study Group. N Engl J Med 2008;358:2545-59

Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes

Glucose Control at baseline and during Follow-up, According to Glucose-Control Strategy



Value							
Standard	7.32	7.30	7.29	7.29	7.31	7.33	7.29
Intensive	7.01	6.93	6.70	6.53	6.50	6.52	6.53



Level				
Standard	8.15	7.84	7.92	7.74
Intensive	7.17	6.47	6.51	6.55

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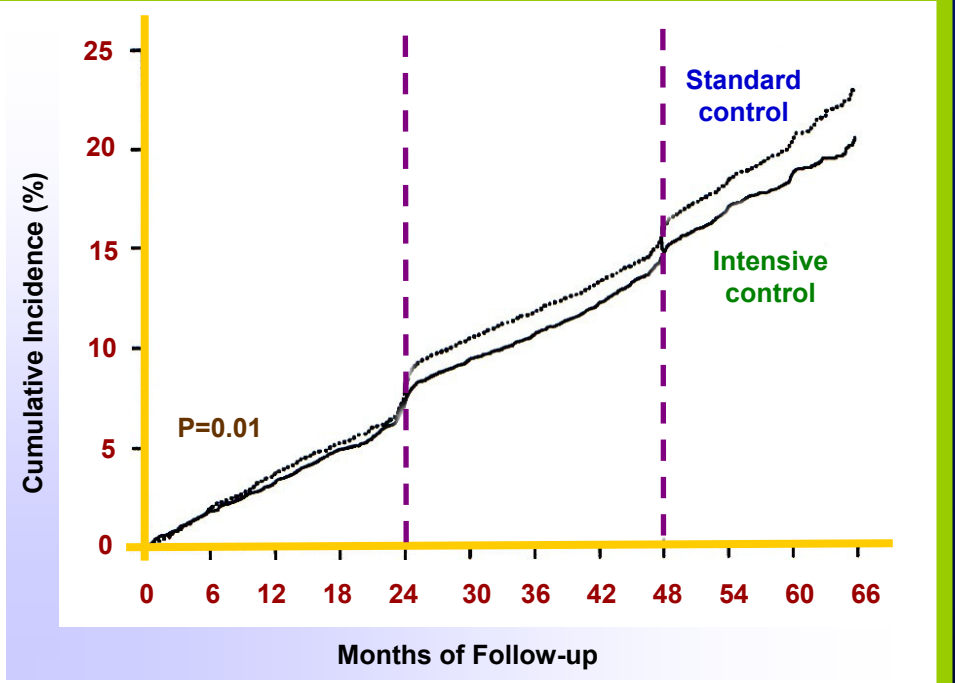
The ADVANCE Collaborative Group. N Engl J Med 2008;358:2560-72

Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes

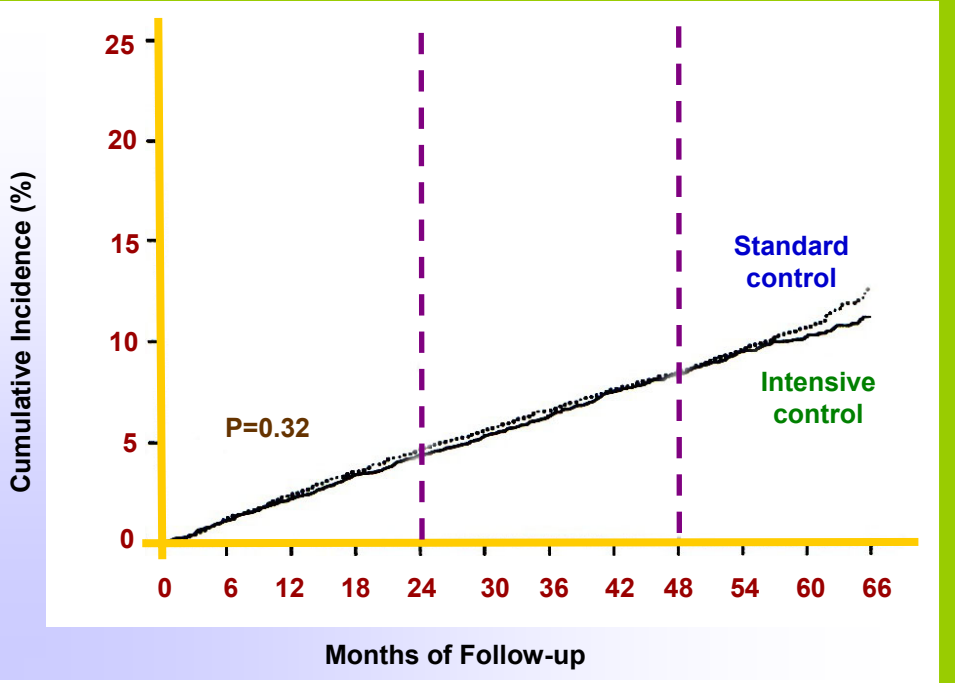
Cumulative incidences of Events, According to Glucose-Control Strategy

Combined Major Macrovascular and Microvascular Events



No. at Risk												
Intensive	5570	5457	5369	5256	5100	4957	4867	4756	4599	4044	1883	447
Standard	5569	5448	5342	5240	5065	4903	4808	4703	4545	3992	1921	470

Major Macrovascular Events



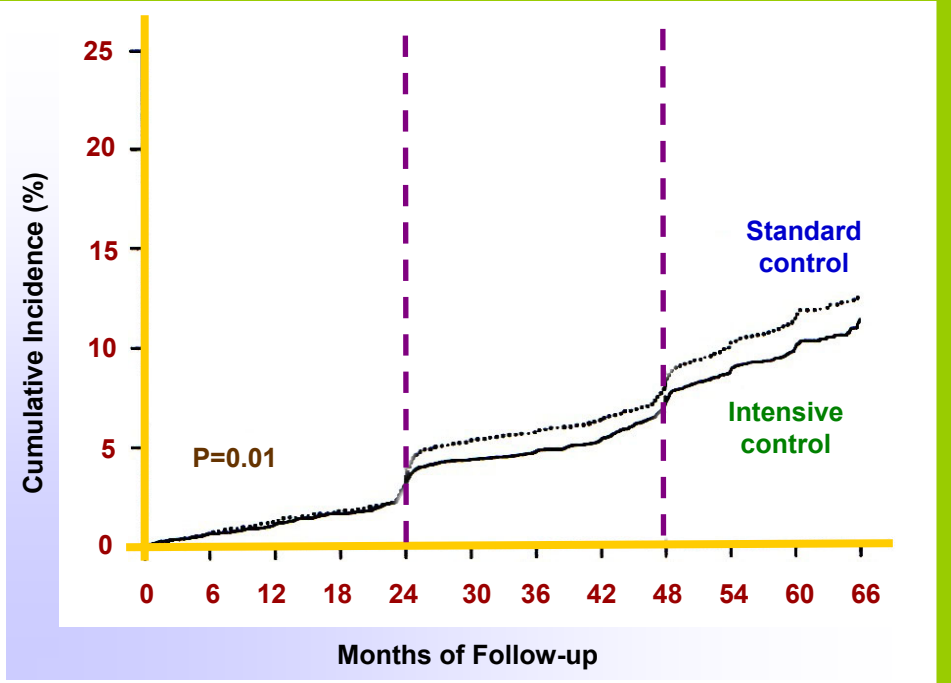
No. at Risk												
Intensive	5570	5494	5428	5338	5256	5176	5097	5005	4927	4396	2071	486
Standard	5569	5486	5413	5330	5237	5163	5084	4995	4922	4385	2108	509

Roy D. et al. N Engl J Med 2008;358:2667-77.

Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes

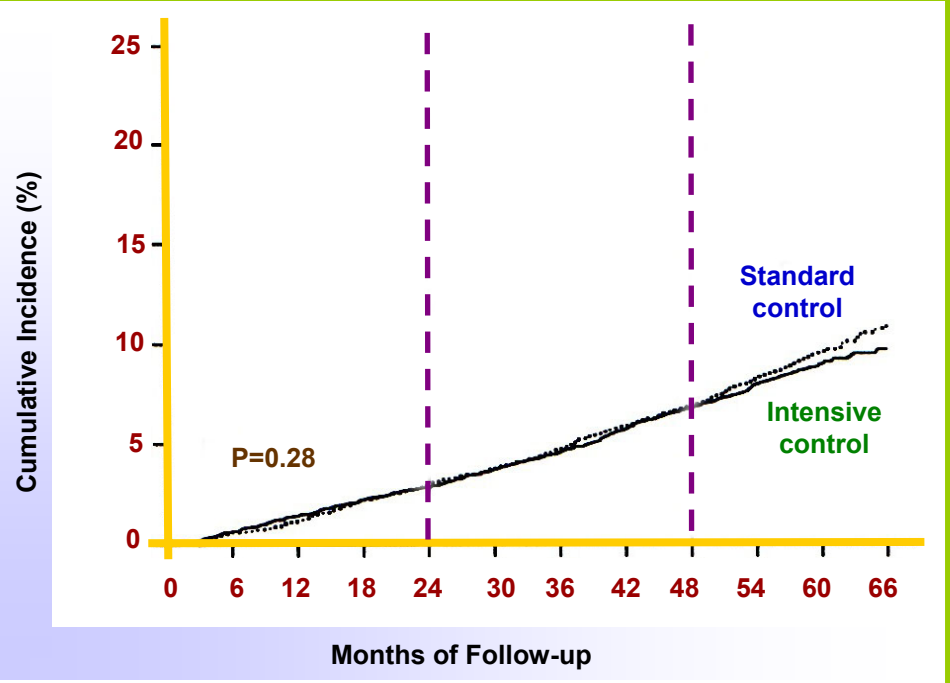
Cumulative incidences of Events, According to Glucose-Control Strategy

Major Microvascular Events



No. at Risk												
Intensive	5571	5495	5430	5358	5233	5120	5055	4968	4824	4258	1992	473
Standard	5569	5498	5431	5353	5207	5069	4995	4911	4764	4204	2024	494

Death from Any Cause



No. at Risk												
Intensive	5571	5533	5490	5444	5411	5361	5312	5246	5189	4653	2211	523
Standard	5569	5537	5503	5445	5399	5354	5301	5237	5178	4643	2240	544

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Denis Roy et al. N Engl J Med 2008;358:2667-77

Intensive Glycemic Control in the ACCORD and ADVANCE Trials

Differences between the ACCORD and ADVANCE Studies

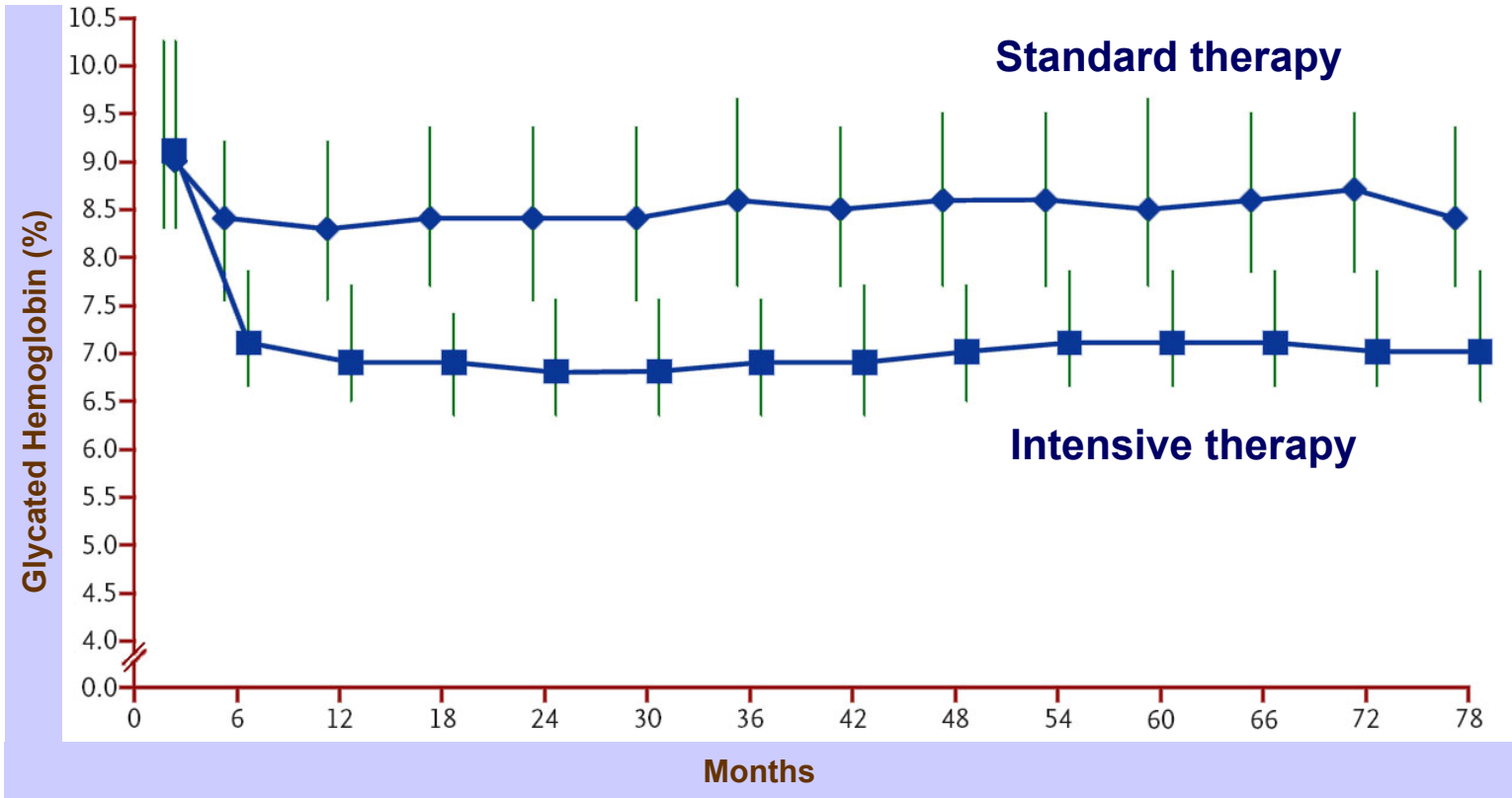
Outcome (intensive vs. standard)		ACCORD	ADVANCE
Median glycated hemoglobin at study end (%)		6.4 vs. 7.5 †	6.4 vs. 7.0 †
Death	From any cause (%)	5.0 vs. 4.0 †	8.9 vs. 9.6
	From cardiovascular causes (%)	2.6 vs. 1.8 †	4.5 vs. 5.2
Nonfatal myocardial infarction (%)		3.6 vs. 4.6 †	2.7 vs. 2.8
Nonfatal stroke (%)		1.3 vs. 1.2 †	3.8 vs. 3.8
Major hypoglycemia requiring assistance (ACCORD), or severe hypoglycemia (ADVANCE) (%/yr)		**3.1 vs. 1.0 †**	**0.7 vs. 0.4**
Weight gain (kg)		3.5 vs. 0.4	0.0 vs. -1.0 †
Current smoking (%)		10 vs. 10	8 vs. 8

†The comparison of the intervention with the standard therapy was significant.

Dluhy RG et al. N Engl J Med 2008;358:2630-33

Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes

Changes in Median Glycated Hemoglobin Levels from Baseline through 78 Months



No. at Risk														
Standard therapy	899	811	812	759	760	727	727	707	688	667	644	472	329	225
Intensive therapy	892	801	805	763	754	729	706	692	668	661	639	489	340	223

The vertical bars represent interquartile ranges

Duckworth W. et al. N Engl J Med 2009;360:129-39

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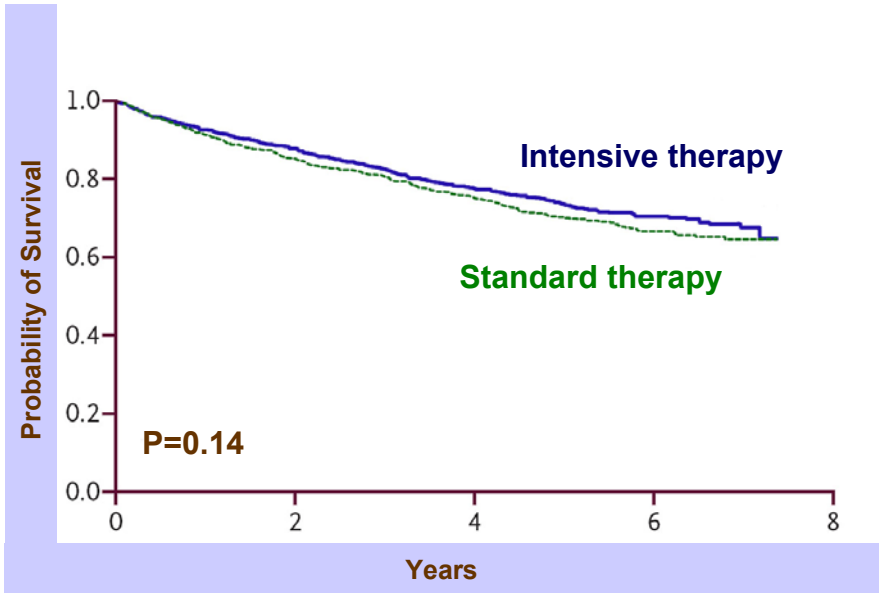
Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes

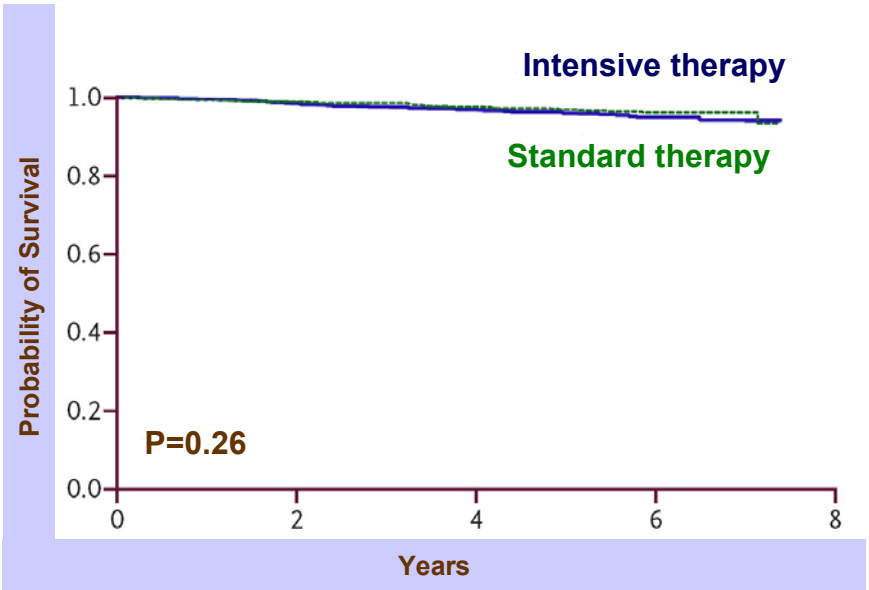
Kaplan–Meier Curves for the Time until the First Occurrence of a Primary or Secondary Outcome

Primary Outcome



No. at Risk									
Standard therapy	899	770	693	637	570	471	240	55	0
Intensive therapy	892	774	707	639	582	510	252	62	0

Death from Cardiovascular Causes



No. at Risk									
Standard therapy	899	833	797	767	724	635	320	75	0
Intensive therapy	892	828	786	746	713	646	337	85	0

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Duckworth W. et al. N Engl J Med 2009;360:129-39

Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes

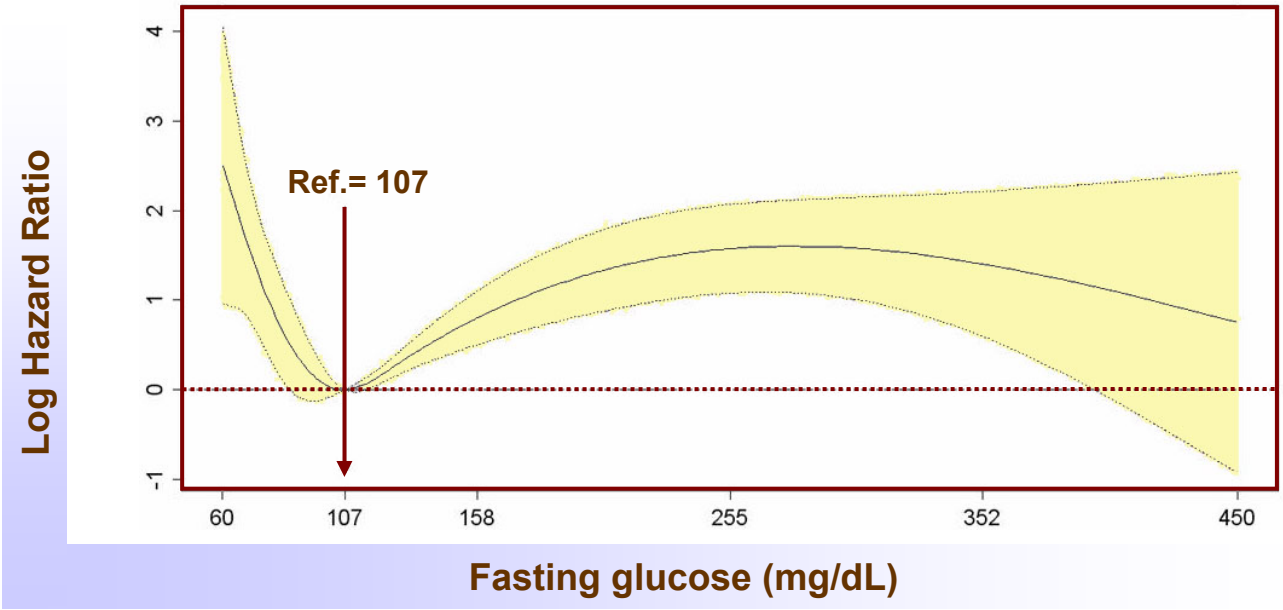
Hypoglycemic Episodes*

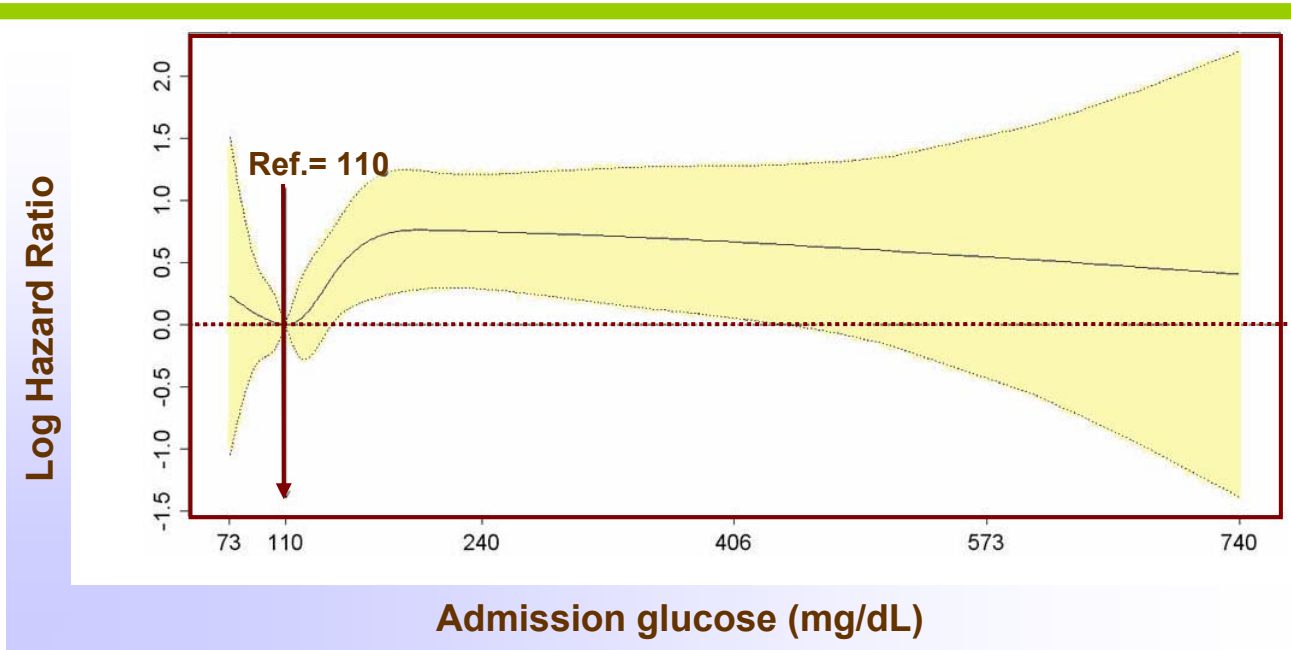
* P<0.001 for all differences between the two groups

Variable		Standard Therapy (N = 899)	Intensive Therapy (N = 892)
		no./100 patient-yr	
Episodes with impaired consciousness		3	9
Episodes with complete loss of consciousness		1	3
Nocturnal episodes		44	152
Total episodes	With symptoms	383	1333
	Without symptoms	49	233
Relieved by food or sugar intake		421	1516
Measurement of blood glucose during episode		348	1392
With documented blood glucose <50 mg/dl (2.8 mmol/liter)		52	203

Duckworth W. et al. N Engl J Med 2009;360:129-39

Glucose and Long-term Mortality in ACS Patients





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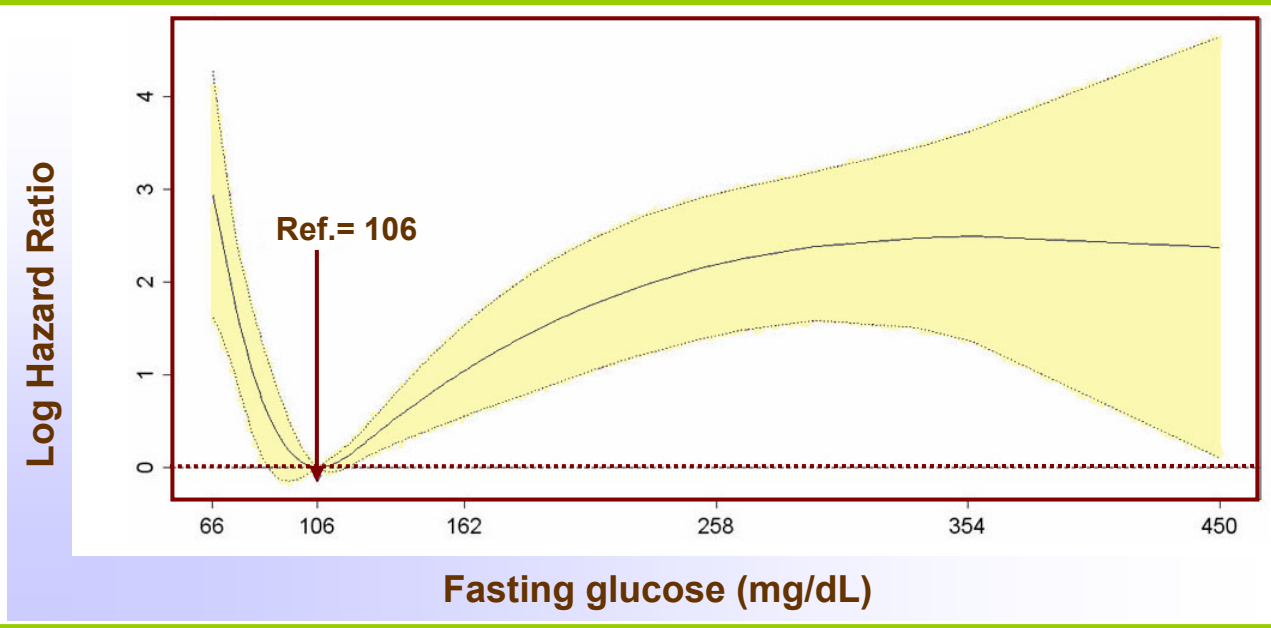
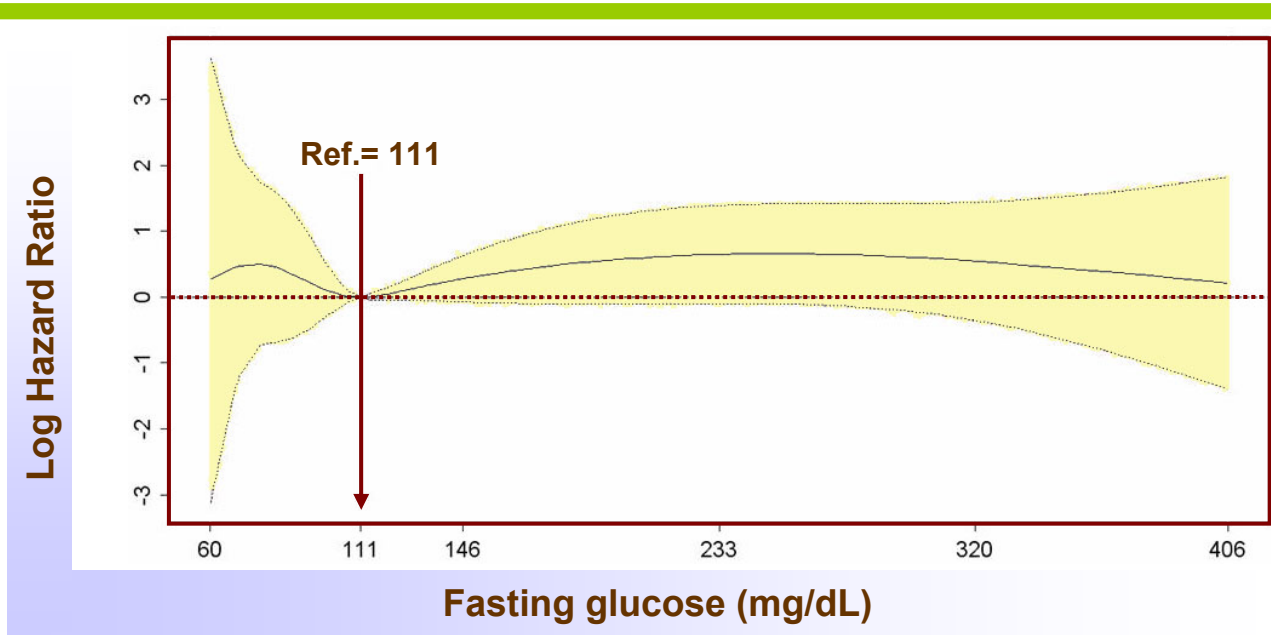
Glucose and Long-term Mortality in ACS Patients

Non-diabetic Patients



Diabetic Patients



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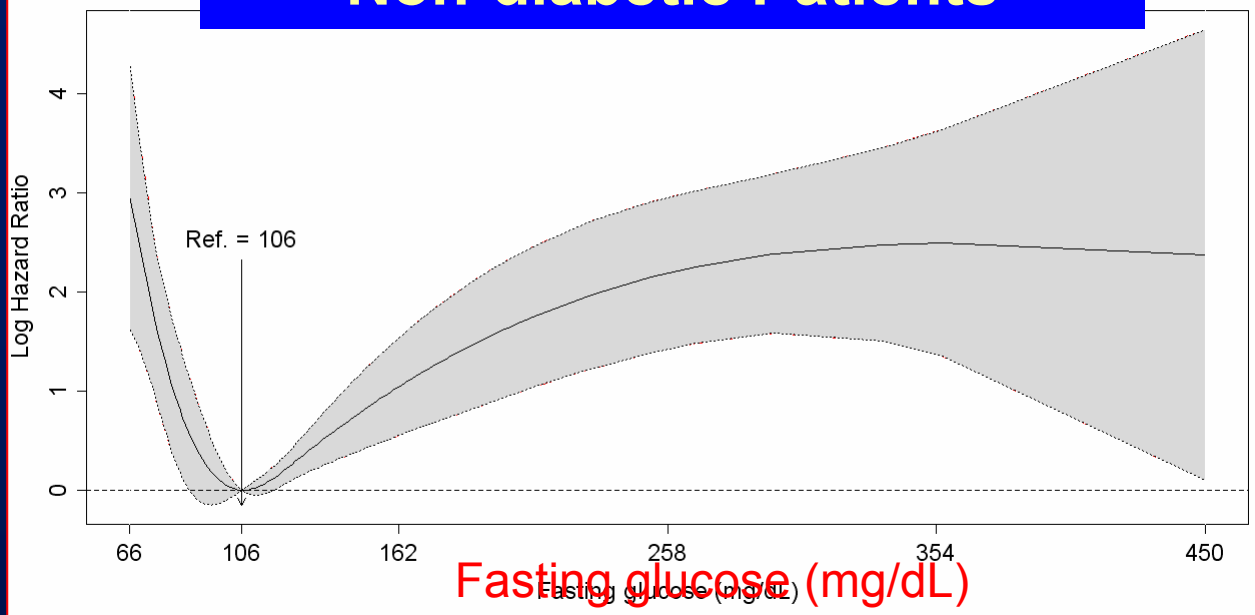
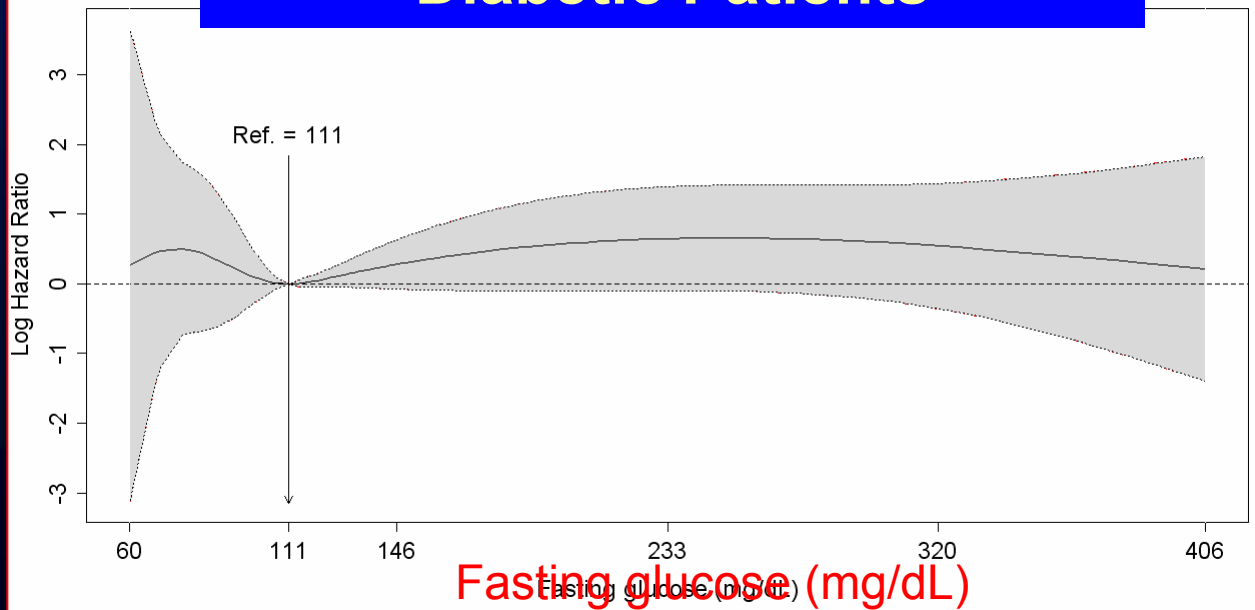
Glucose and Long-term Mortality in ACS Patients

Non-diabetic Patients



Fasting glucose (mg/dL)

Diabetic Patients



Fasting glucose (mg/dL)

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FDA News

FDA U.S. Food and Drug Administration Department of Health and Human Services

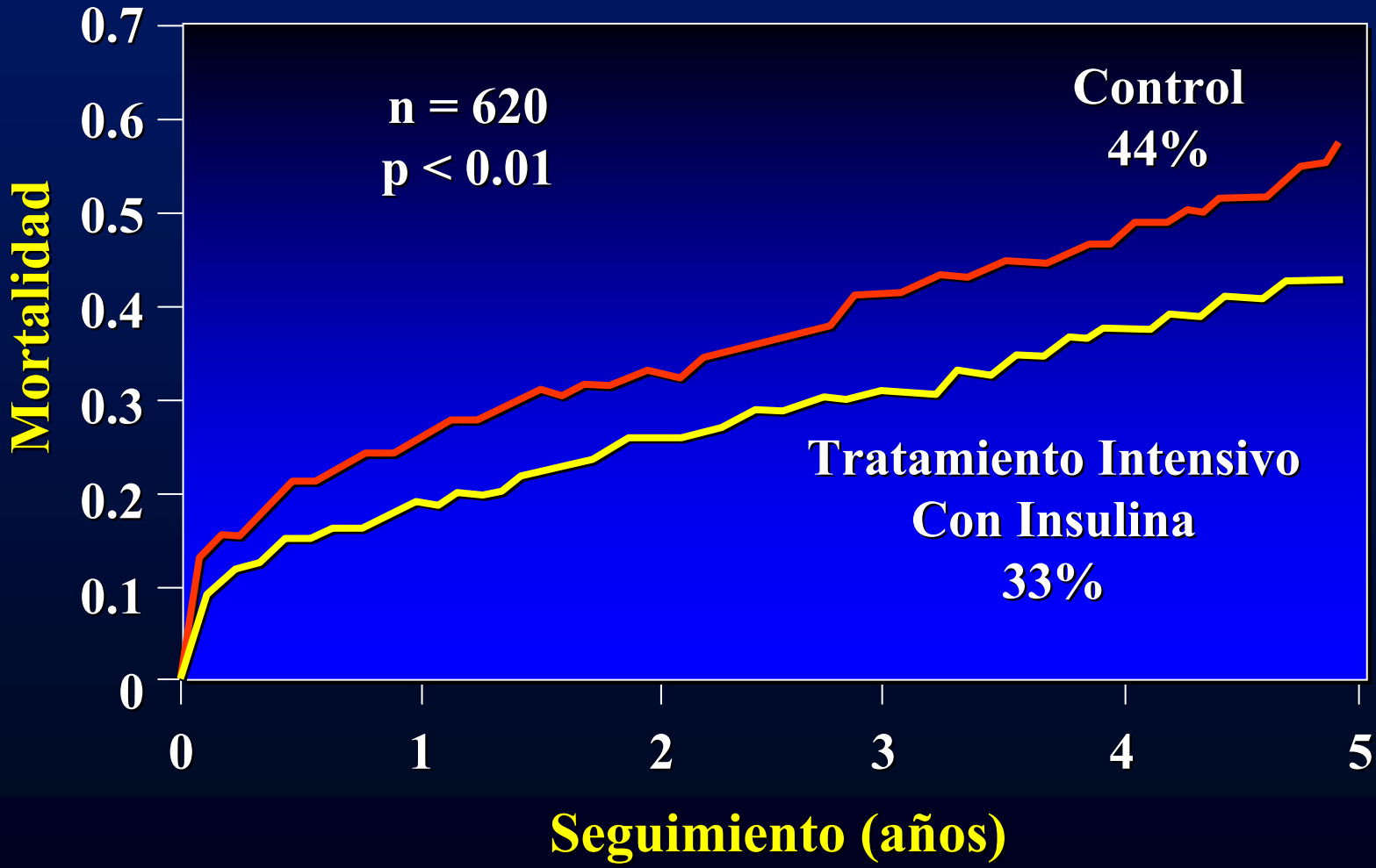
FDA Decision Nov 14

To date, no oral anti-diabetes drug has been conclusively shown to reduce cardiovascular risk. Consequently, the agency also will be requesting that labeling of all approved oral anti-diabetes drugs contain language describing the lack of data showing this benefit.

http://www.fda.gov/bbs/topics/NEWS/2007/NEW01743.html

TRATAMIENTO CON INSULINA Y SUPERVIVENCIA TRAS IAM

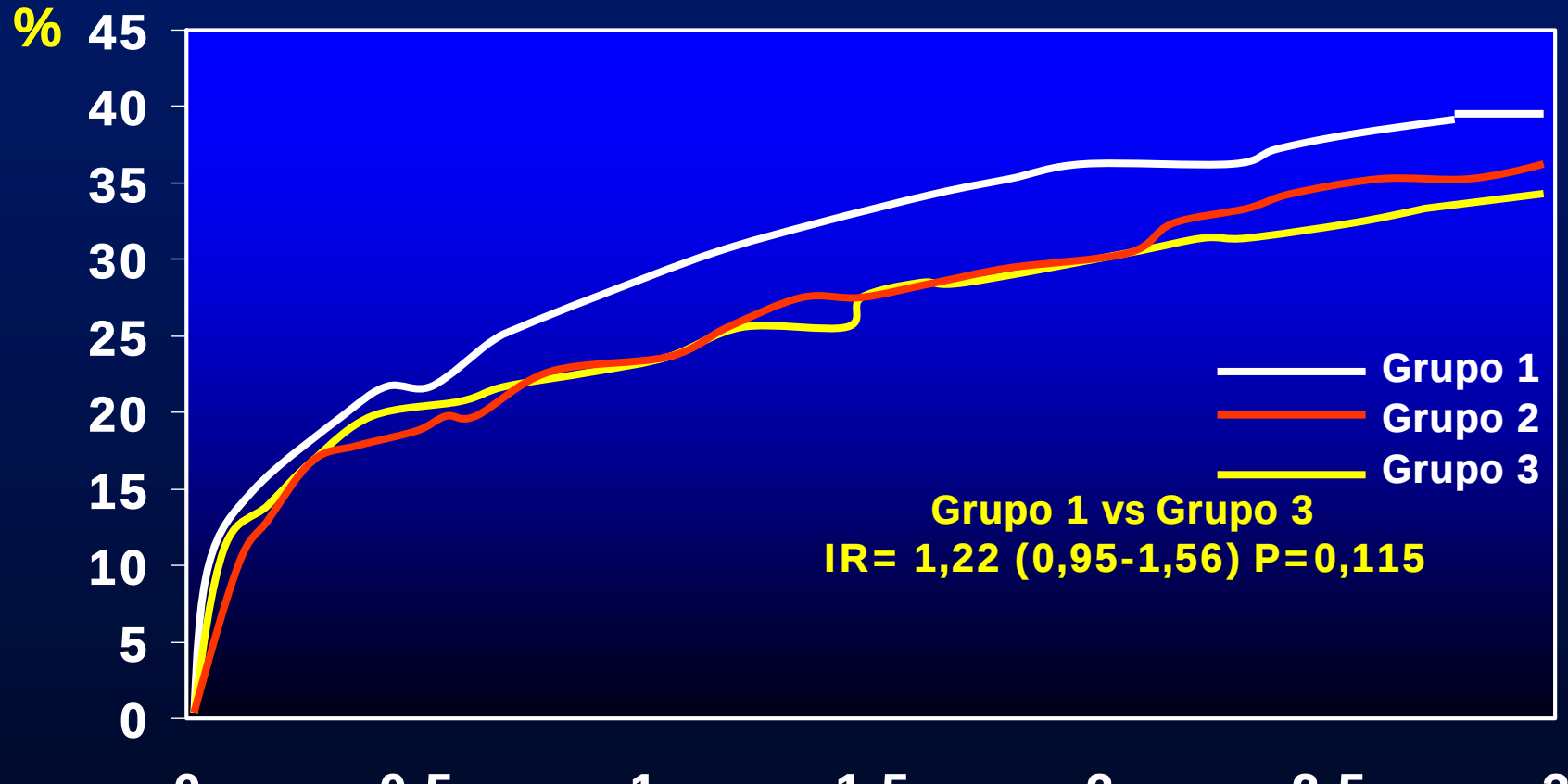
IAM < 24h
N=620
Glucemia > 11 mmol/l
Intensivo:
Infusión Insulina (100%)
Seguida de sc (87%)
Control:
Practica clínica
43% insulina sc



DIGAMI

BMJ 1997;314:1512

Estudio DIGAMI II.



Nº de riesgo	0	0,5	1	1,5	2	2,5	3
Grupo 1	474	367	299	254	202	154	87
Grupo 2	473	381	317	261	225	170	91
Grupo 3	306	241	214	175	145	119	80

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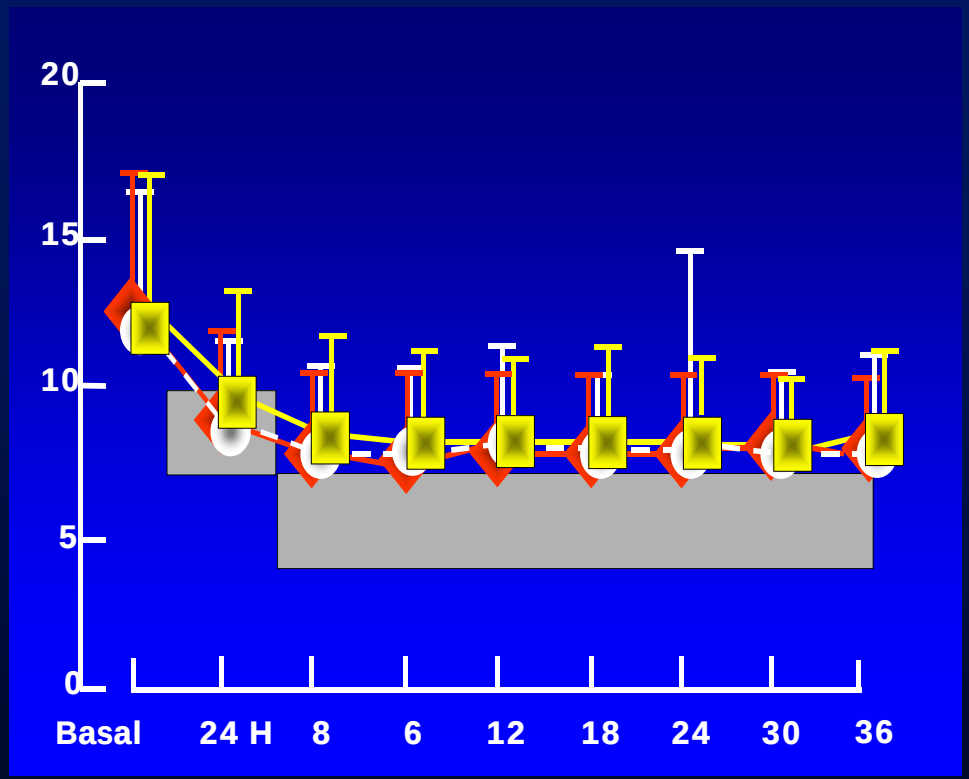
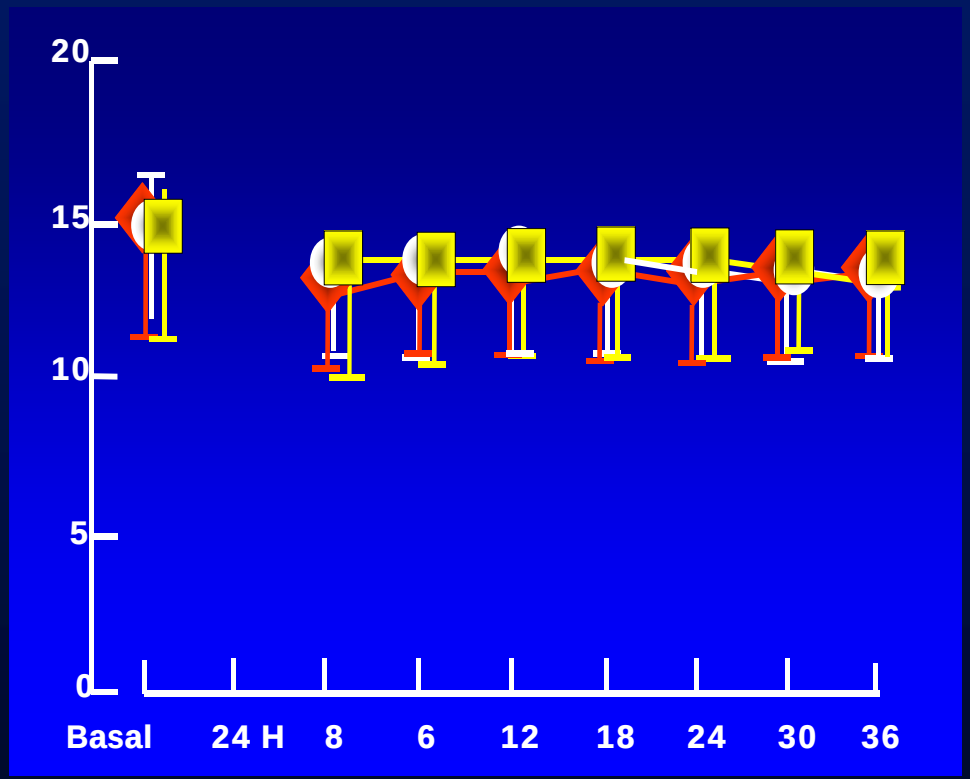
Malmberg, k, et al Eur Heart j. 2005;206:650-661

Estudio DIGAMI II. Control Metabólico





meses

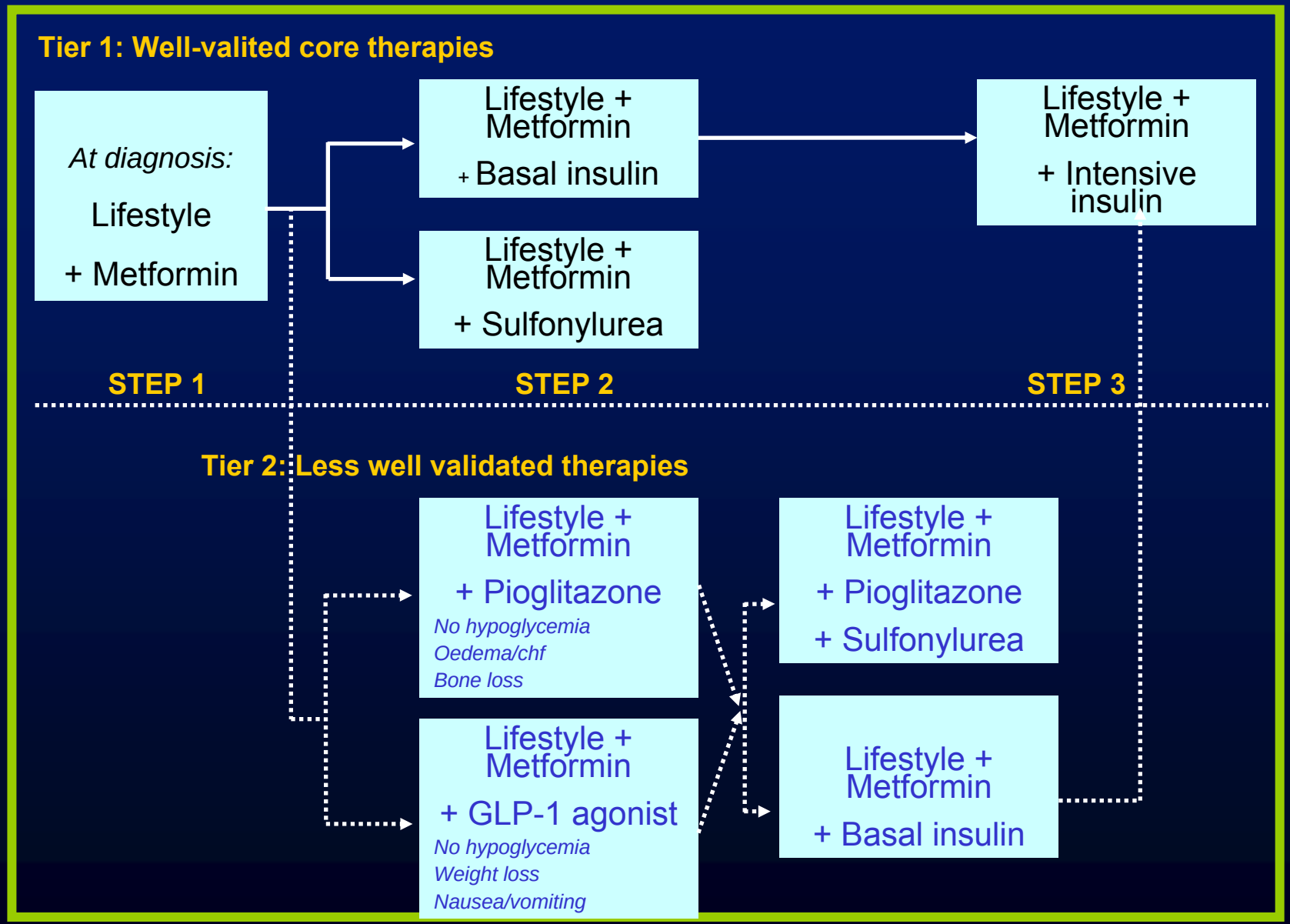
Malmberg, k, et al Eur Heart J. 2005;206:650-661

TRATAMIENTO INTENSIVO

RECOMENDACIÓN	CLASE	NIVEL
Control estricto de glucosa con insulina perfusión mejora mortalidad y morbilidad de pacientes sometidos a cirugía cardíaca	I	B
Control estricto de glucosa con insulina perfusión mejora mortalidad y morbilidad de pacientes críticos	I	A

Guidelines on diabetes, pre-diabetes, and cardiovascular diseases. Eur Heart J 2007; 28, 88–136

Medical Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy



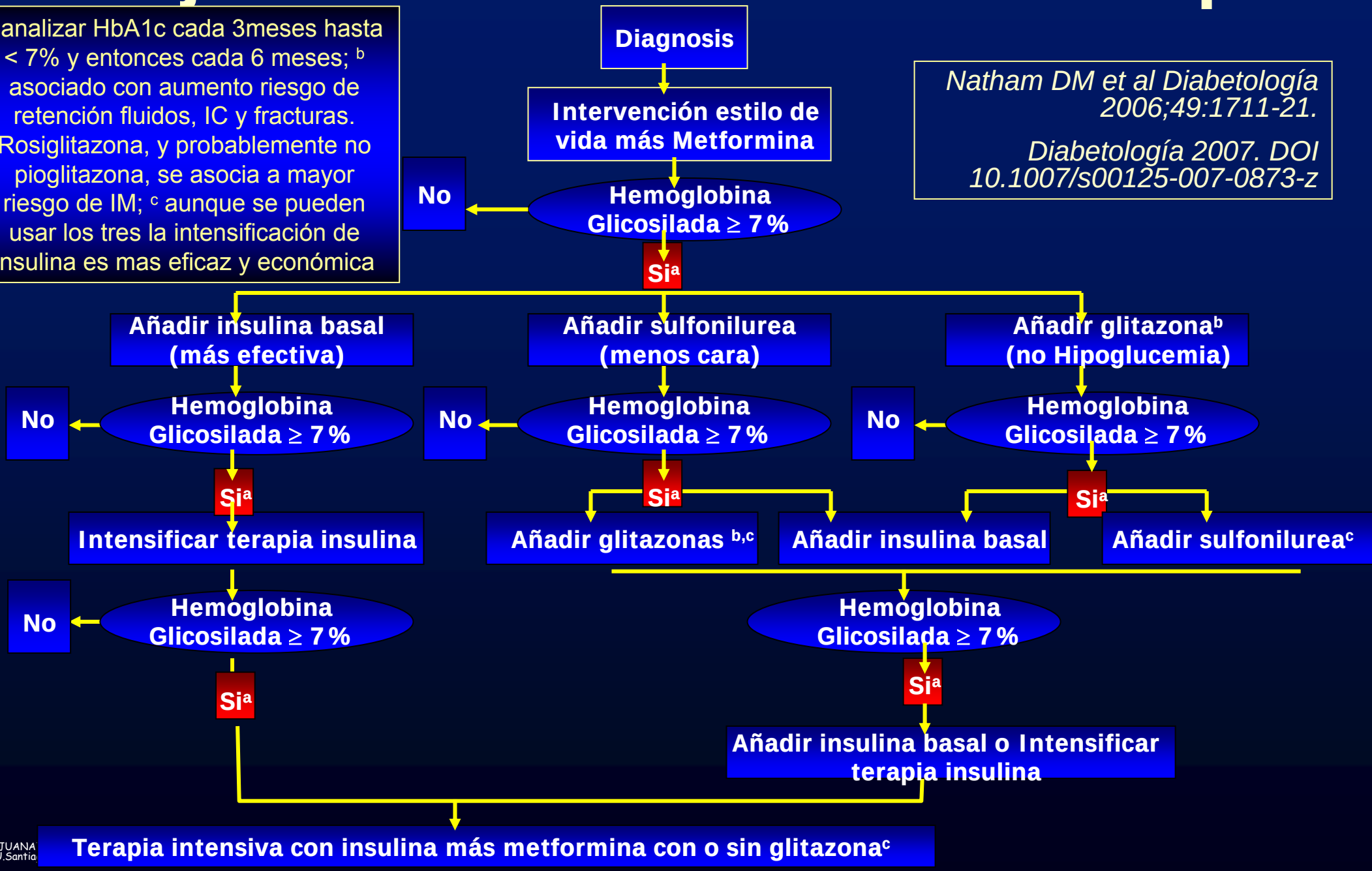
Algorithm for the metabolic management of type 2 diabetes

Nathan DM et al. Diabetes Care 2008; 31:1-11

J.R.G. JUANATEY
C.H.U.Santiago

Manejo Metabólico de la Diabetes Tipo 2

[a] analizar HbA1c cada 3meses hasta < 7% y entonces cada 6 meses; [b] asociado con aumento riesgo de retención fluidos, IC y fracturas. Rosiglitazona, y probablemente no pioglitazona, se asocia a mayor riesgo de IM; [c] aunque se pueden usar los tres la intensificación de insulina es mas eficaz y económica



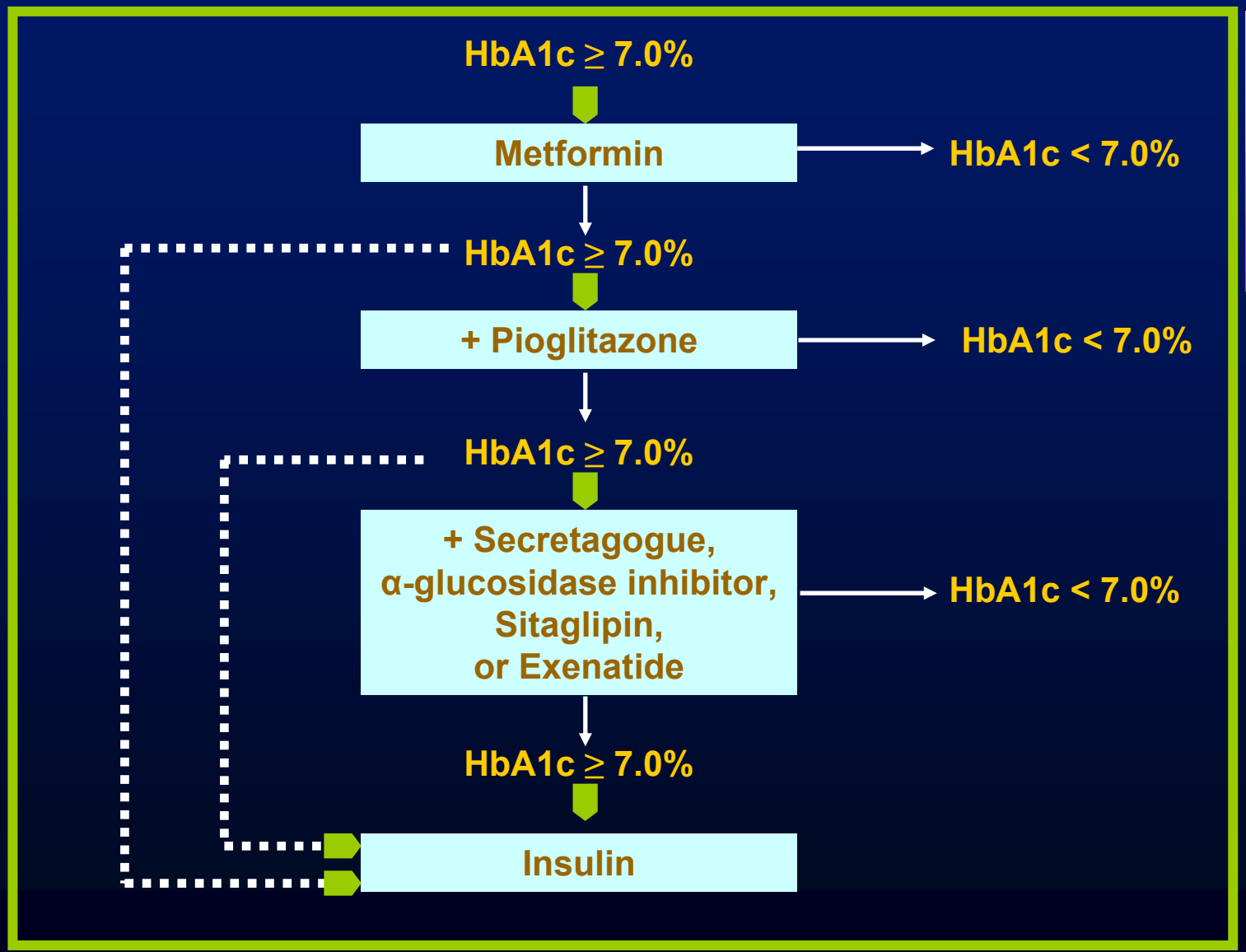
Natham DM et al Diabetología 2006;49:1711-21.

Diabetología 2007. DOI 10.1007/s00125-007-0873-z

J.R.G. JUANA
C.H.U.Santia

New Drugs for the Treatment of Diabetes

Part II: Incretin-Based Therapy and Beyond



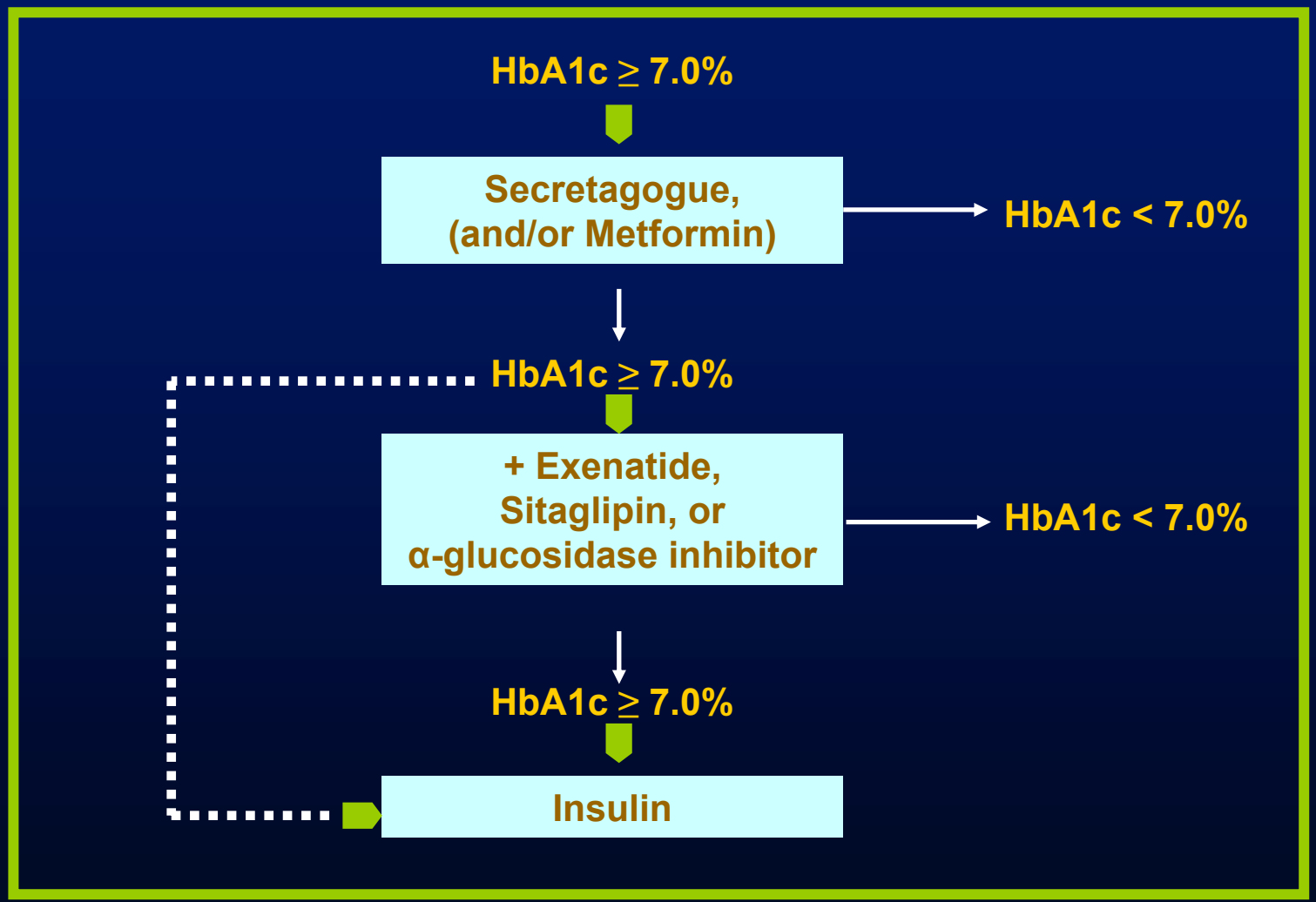
Proposed antihyperglycemic strategy in the patient with T2DM and CAD

J.R.G. JUANATEY
C.H.U.Santiago

Inzucchi SE et al. Circulation. 2008;117:574-584.

New Drugs for the Treatment of Diabetes

Part II: Incretin-Based Therapy and Beyond



Proposed antihyperglycemic strategy in the patient with T2DM and HF

Inzucchi SE et al. Circulation. 2008;117:574-584.

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C.H.U.Santiago

Tasas de Infarto de Miocardio y de Mortalidad Cardiovascular

Nissen S, et al. N Engl J Med 2007;356

Estudio	Rosiglitazona nº eventos/nº total (%)	Grupo Control nº eventos/nº total (%)	Odds Ratio (IC 95%)	p
INFARTO DE MIOCARDIO				
Pequeños Ensayos	44/10280 (0.43)	22/6105 (0.36)	1.45 (0.88 -2.39)	0.15
DREAM	15/2635 (0.57)	9/2634 (0.34)	1.65 (0.74 – 3.68)	0.22
ADOPT	27/1456 (1.85)	41/2895 (1.44)	1.33 (0.80 – 2.21)	0.27
Global			1.43 (1.03 – 1.98)	0.03
MORTALIDAD CARDIOVASCULAR				
Pequeños Ensayos	25/6557 (0.38)	7/3700 (0.19)	2.40 (1.17 – 4.91)	0.02
DREAM	12/2365 (0.51)	10/2634 (0.38)	1.20 (0.52 – 2.78)	0.67
ADOPT	2/1456 (0.14)	5/2854 (0.18)	0.80 (0.17 – 3.86)	0.78
Global			1.64 (0.98 – 2.74)	0.06

"The Rosiglitazone Story. Lessons from and FDA Advisory Committee Meeting"
WellPoint Observational Study

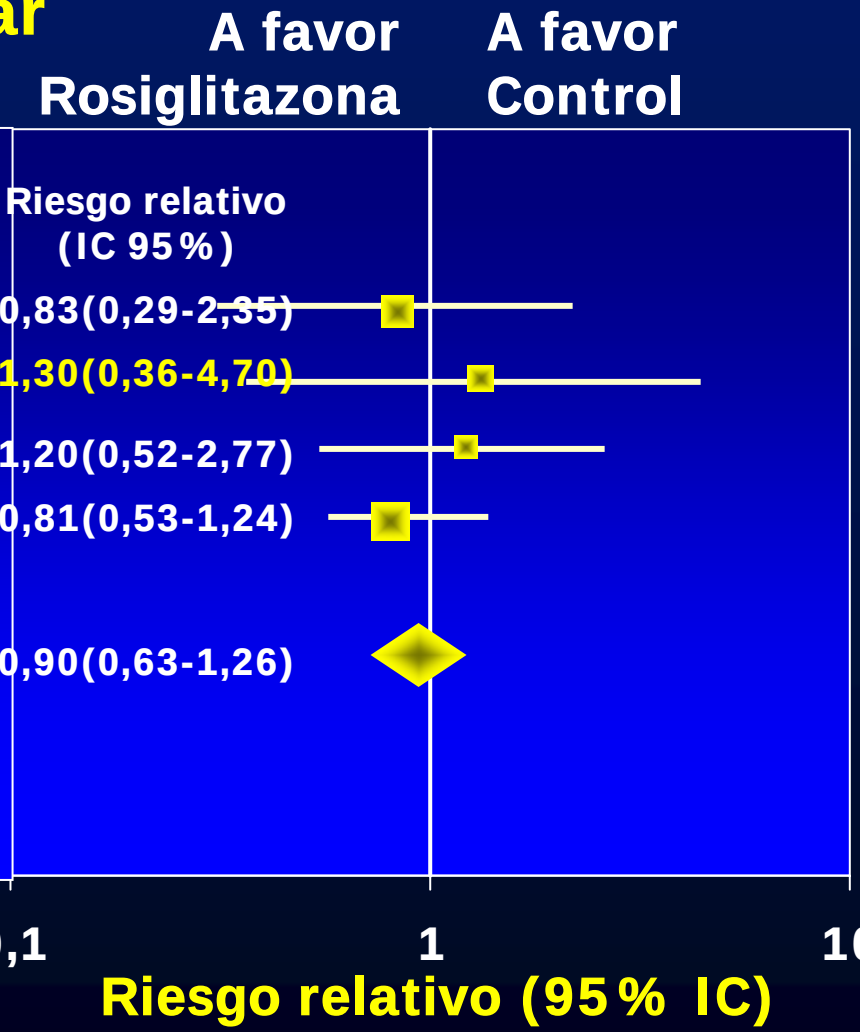
Fármaco	Nº Pac total	IAM			
		Nº de enferm	Incidencia por 100000 pac/año	IR (IC 95%)	Valor P
Rosiglitazona	22050	212	0,73	1,029(0,886-1,194)	0,710
Pioglitazona	23768	232	0,74	1,044(0,905-1,205)	0,553
Otros antidiabéticos orales	120771	866	0,72	1,000	

Rosen C J N Engl J Med 2007

Riesgo de Enfermedades Cardiovasculares a Largo Plazo con Rosiglitazona

Mortalidad Cardiovascular

Fuente	Rosiglitazona	Control	Peso %	Riesgo relativo (IC 95%)
	Rosiglitazona Nº de enf. /Total (%)			
Kahn et al, 2006	5/1456(0,3)	12/2895(0,4)	11,83	0,83(0,29-2,35)
Dargie et al, 2007	5/110(4,5)	4/114(3,6)	5,79	1,30(0,36-4,70)
Gerstein et al , 2006	12/2635(0,5)	10/2634(0,4)	14,73	1,20(0,52-2,77)
Home et al, 2007	37/2220(1,7)	46/2227(2,1)	67,65	0,81(0,53-1,24)
Total (IC 95%)	6421	7870	100,00	0,90(0,63-1,26)



Total enfermedades: 59 (rosiglitazona), 72 (control)

Test de heterogeneidad; χ^2_3= 1,03 (P=0,79), I^2=0%

Tests efecto total; Z=0,63 (P=0,53)

Singh S et al JAMA 2007,10:1189-1195

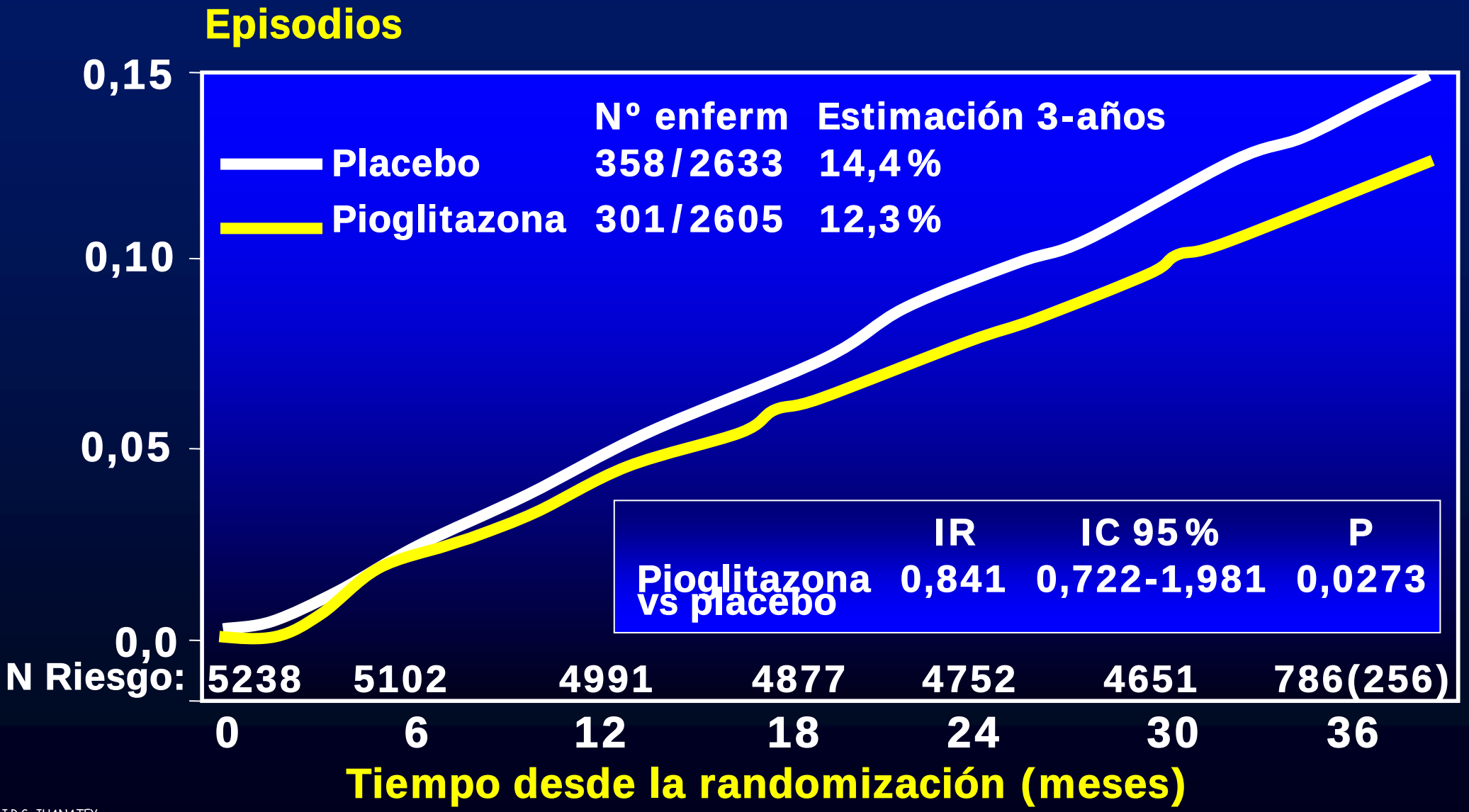
J.R.G. JUANATEY
C.H.U.Santiago

Rosiglitazona y Riesgo CVC. Un Análisis Intermedio del Estudio RECORD.

Variable	Grupo Rosiglitazona (N=2220)	Grupo control (N=2227)	IR (IC 95%)	Valor P
Enfermedades adjudicadas	n° pacientes			
Objetivo primario	217	202	1,08(0,89-1,31)	0,43
Muerte				
Causas CV	29	35	0,83(0,51-1,36)	0,46
Cq causa	74	80	0,93(0,67-1,27)	0,63
IAM	43	37	1,16(0,75-1,81)	0,50
IC Congestiva	38	17	2,24(1,27-3,97)	0,006
Muerte por causas CV, IAM e ictus	93	96	0,97(0,73-1,29)	0,83

Home P D et al, N Engl J Med 2007;357-1

Estudio ProACTIVE. Muerte, IM (incluso Silente) o Ictus



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Rosiglitazona y Riesgo CVC. Un Análisis Intermedio del Estudio RECORD.

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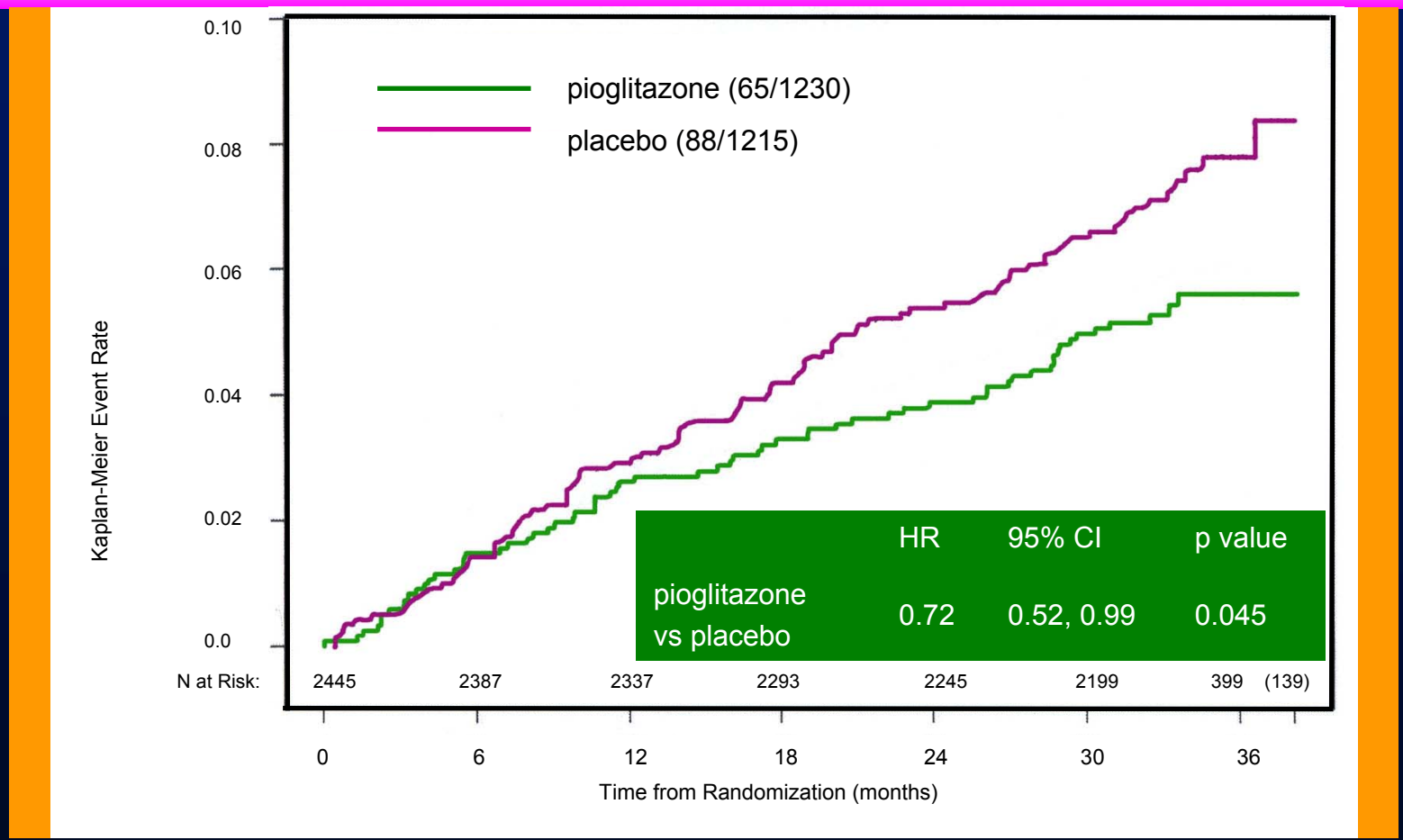
Home P D et al, N Engl J Med 2007;357-1

The Effect of Pioglitazone on Recurrent Myocardial Infarction in 2,445 Patients With Type 2 Diabetes and Previous Myocardial Infarction

Time to Fatal/Nonfatal MI (Excluding Silent MI)



The solid line represents the pioglitazone group; the dashed line represents the placebo group. CI = confidence interval; HR = hazard ratio.

Erdmann E et al. Journal of the American College of Cardiology; Vol. 49, No.17, 2007

Comparison of Cardiovascular Outcomes in Elderly Patients With Diabetes Who Initiated Rosiglitazone vs Pioglitazone Therapy

Associations of New Pioglitazone vs New Rosiglitazone Use and Subsequent Clinical Outcomes (On-Drug Exposure Models)

	Exposure*	No. of Patients	No. of Events	Event Rates per 1000 Person-Years	IRR (95% CI)	
					Crude	Adjusted
All-cause mortality	Pioglitazone	14 260	885	59.7		
	Rosiglitazone	14 101	984	69.2	1.17 (1.06-1.28)	1.15 (1.05-1.26)
MI	Pioglitazone	14 260	363	24.7		
	Rosiglitazone	14 101	374	26.5	1.10 (0.95-1.27)	1.08 (0.93-1.25)
Hospitalization for CHF	Pioglitazone	14 260	614	42.0		
	Rosiglitazone	14 101	645	46.0	1.12 (1.00-1.25)	1.13 (1.01-1.26)
Prior CHF	Pioglitazone	3009	317	127.5		
	Rosiglitazone	3163	320	129.4	1.01 (0.87-1.18)	1.04 (0.89-1.22)
No prior CHF	Pioglitazone	11 251	297	24.5		
	Rosiglitazone	10 938	325	28.1	1.19 (1.02-1.40)	1.21 (1.03-1.42)

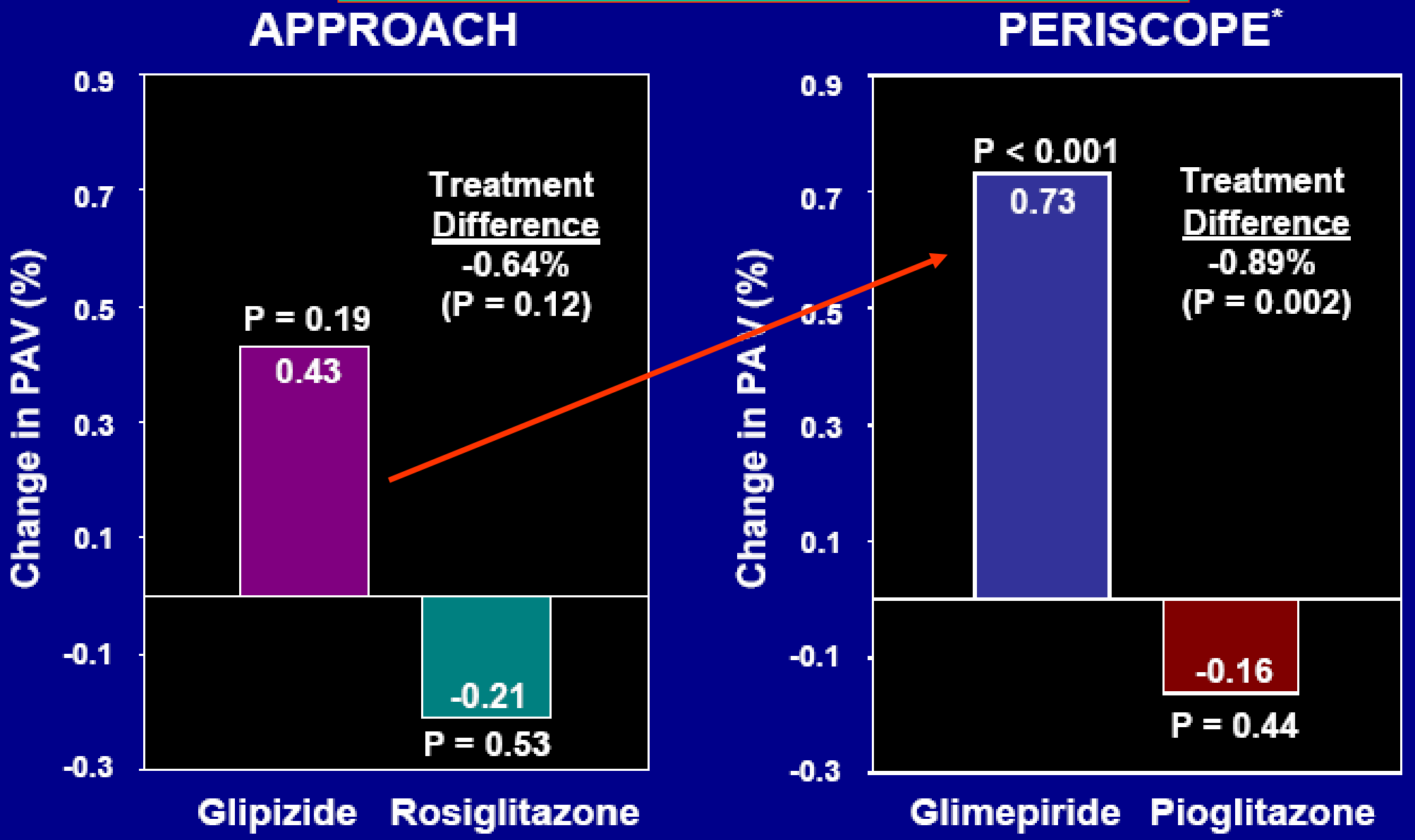
CHF, congestive heart failure; CI, confidence interval; IRR, incidence rate ratio; MI, myocardial infarction.

*Pioglitazone is pioglitazone hydrochloride and rosiglitazone is rosiglitazone maleate.

Winkelmayer WC et al. Arch Intern Med. 2008;168:2368-2375

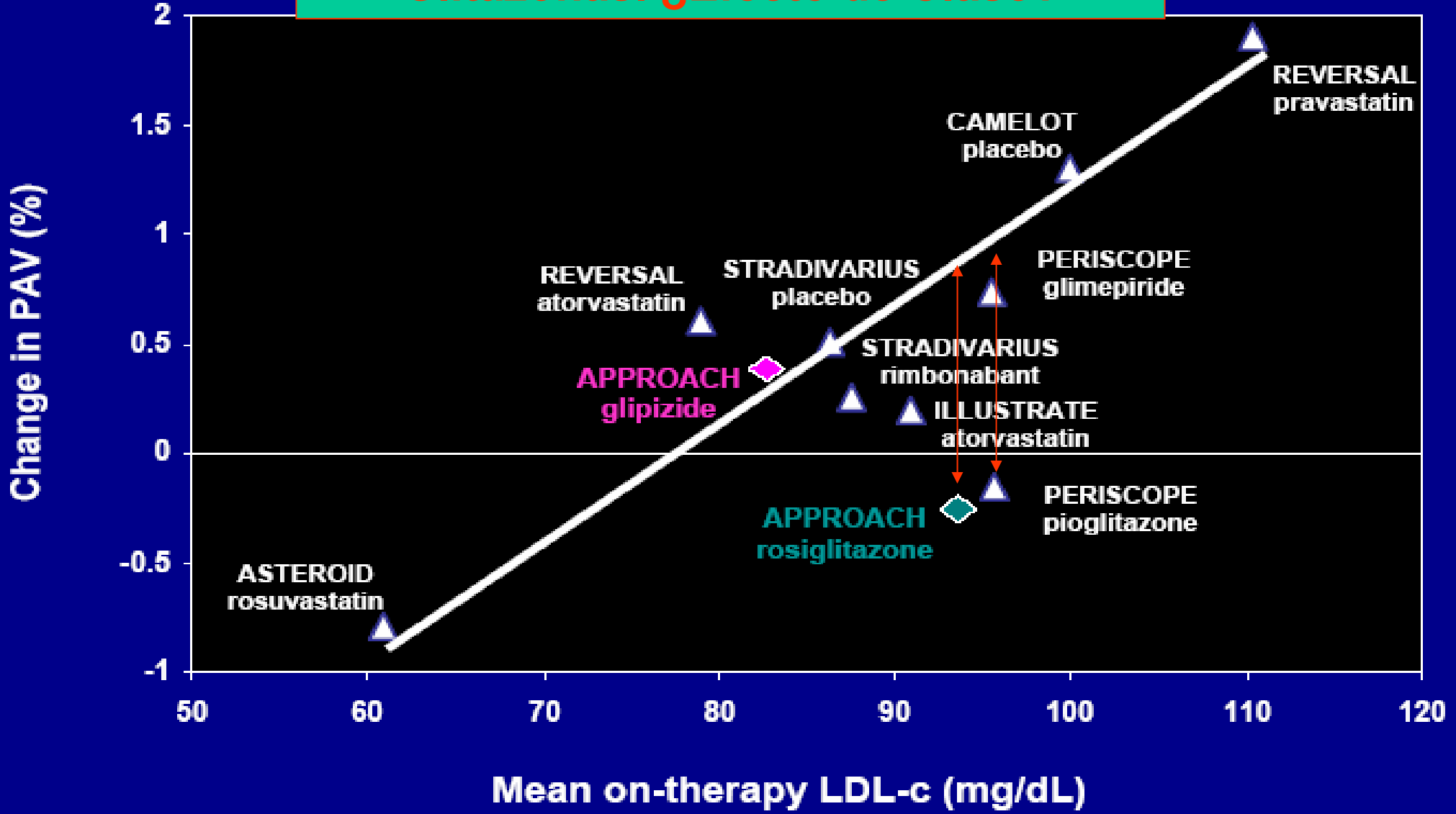
Comparison of Primary Endpoints

Glitazonas. ¿Efecto de Clase?



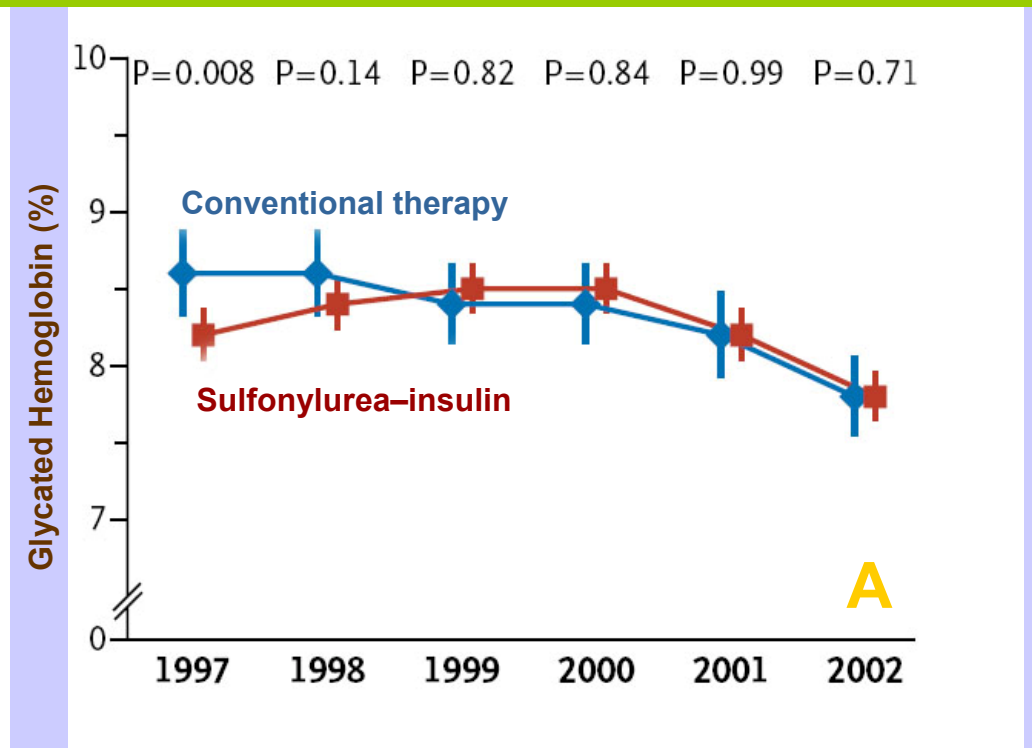
Other IVUS Trials

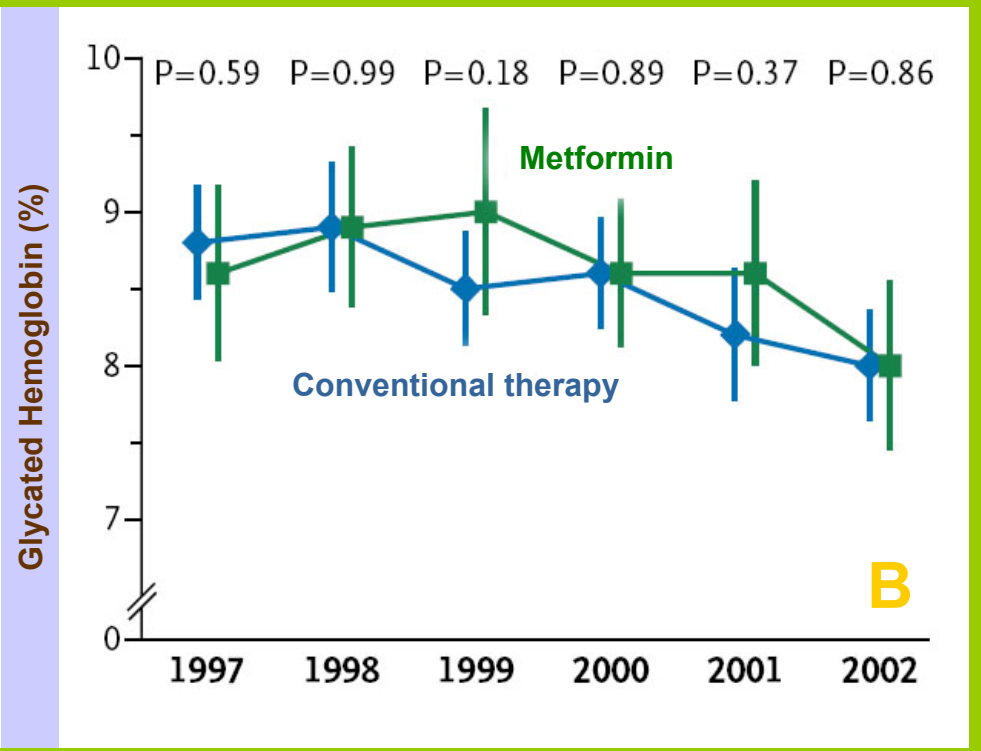
Glitazonas. ¿Efecto de Clase?



10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes. UKPDS Follow-up

Mean Glycated Hemoglobin Levels





Glycated hemoglobin levels for patients who were originally assigned to receive either sulfonylurea–insulin or conventional therapy (Panel A) or metformin or conventional therapy (Panel B) are shown.

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Holman RR et al. N Engl J Med 2008;359

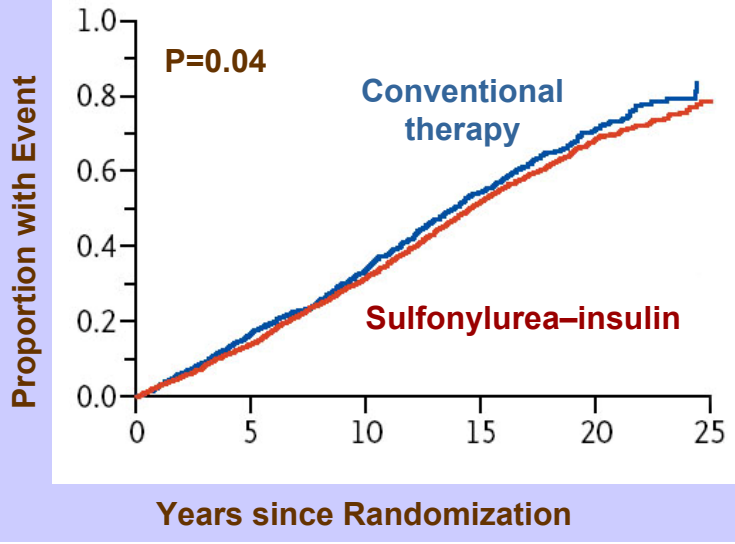
10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes

Kaplan–Meier Curves for Four Prespecified Aggregate Clinical Outcomes

Any Diabetes-Related End Point

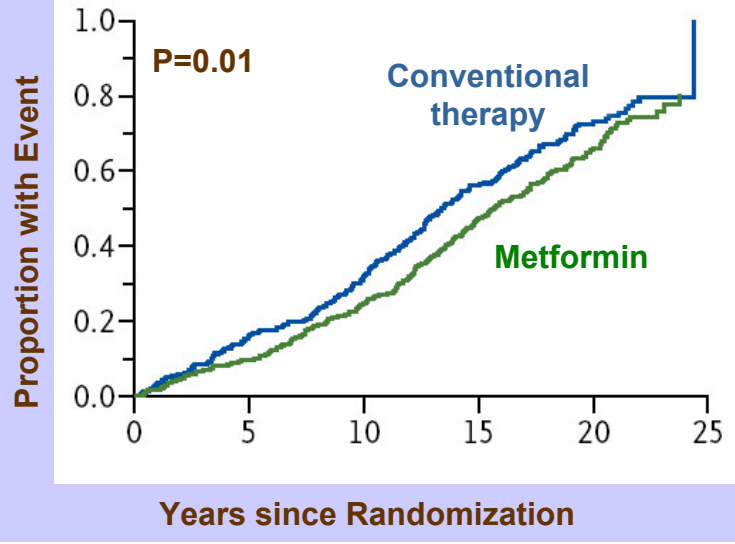
Any Diabetes-Related End Point

A



No. at Risk						
Conventional therapy	1138	913	679	370	104	5
Sulfonylurea–insulin	2729	2270	1692	933	277	32

B



No. at Risk						
Conventional therapy	411	333	255	132	45	2
Metformin	342	300	236	144	62	7

The proportions of patients in the United Kingdom Prospective Diabetes Study who had any diabetes-related end point (Panels A and B), myocardial infarction (Panels C and D) or who died from any cause (Panels E and F) are shown for the sulfonylurea–insulin group versus the conventional-therapy group and for the metformin group versus the conventional-therapy group.

Holman RR et al. N Engl J Med 2008;359

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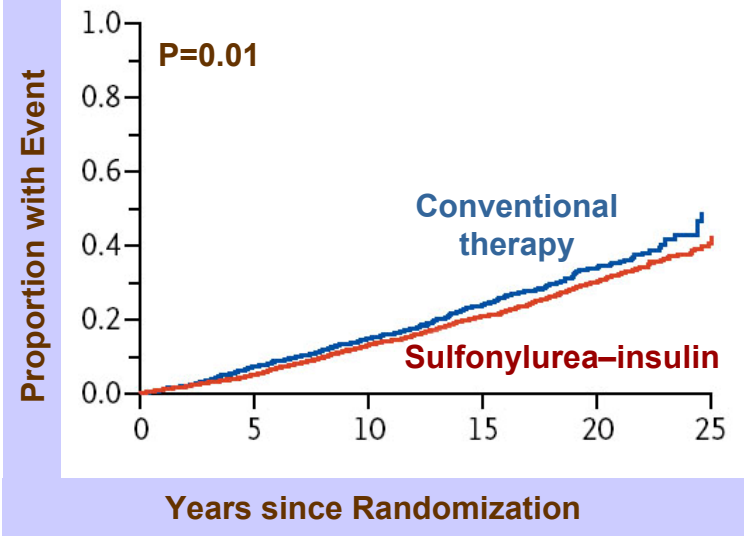
10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes

Kaplan–Meier Curves for Four Prespecified Aggregate Clinical Outcomes

Myocardial Infarction

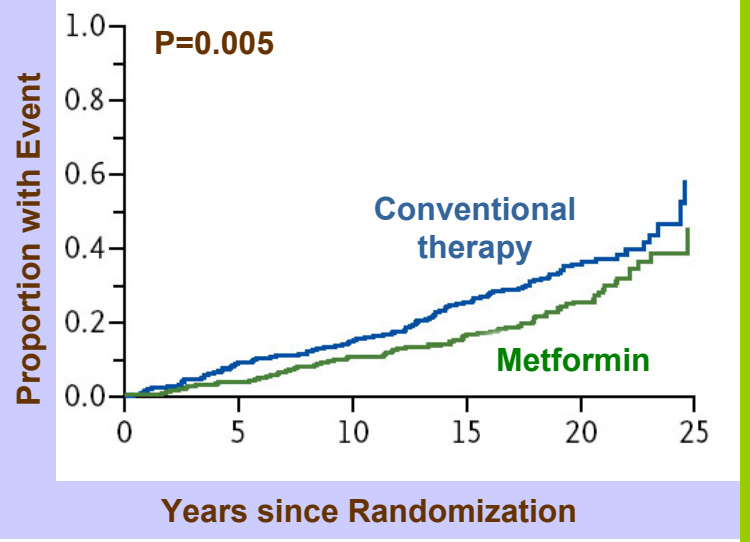
Myocardial Infarction

C



No. at Risk						
Conventional therapy	1138	1013	857	578	221	20
Sulfonylurea–insulin	2729	2488	2097	1459	577	66

D



No. at Risk						
Conventional therapy	411	360	311	213	95	4
Metformin	342	317	274	214	106	16

The proportions of patients in the United Kingdom Prospective Diabetes Study who had any diabetes-related end point (Panels A and B), myocardial infarction (Panels C and D) or who died from any cause (Panels E and F) are shown for the sulfonylurea–insulin group versus the conventional-therapy group and for the metformin group versus the conventional-therapy group.

J.R.G. JUANATEY
C.H.U.Santiago

Rury R. Holman et al. N Engl J Med 2008;359

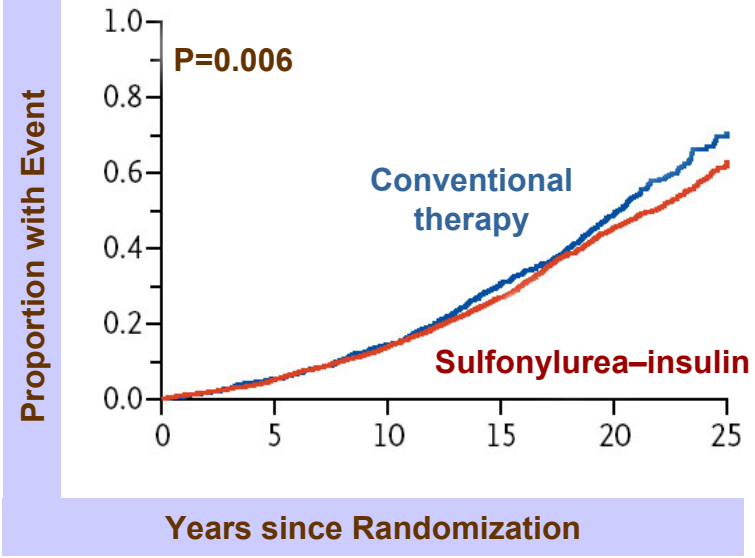
10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes

Kaplan–Meier Curves for Four Prespecified Aggregate Clinical Outcomes

Death from Any Cause

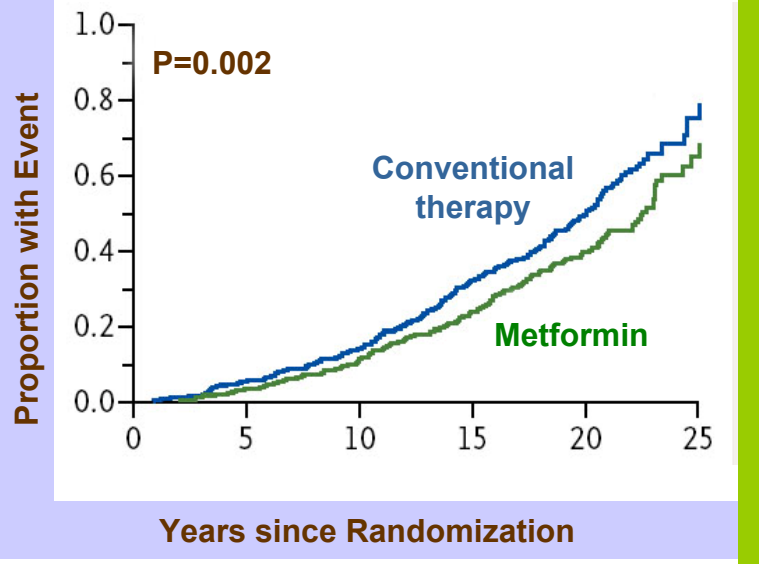
Death from Any Cause

E



No. at Risk						
Conventional therapy	1138	1066	939	665	270	28
Sulfonylurea–insulin	2279	2573	2276	1675	680	83

F



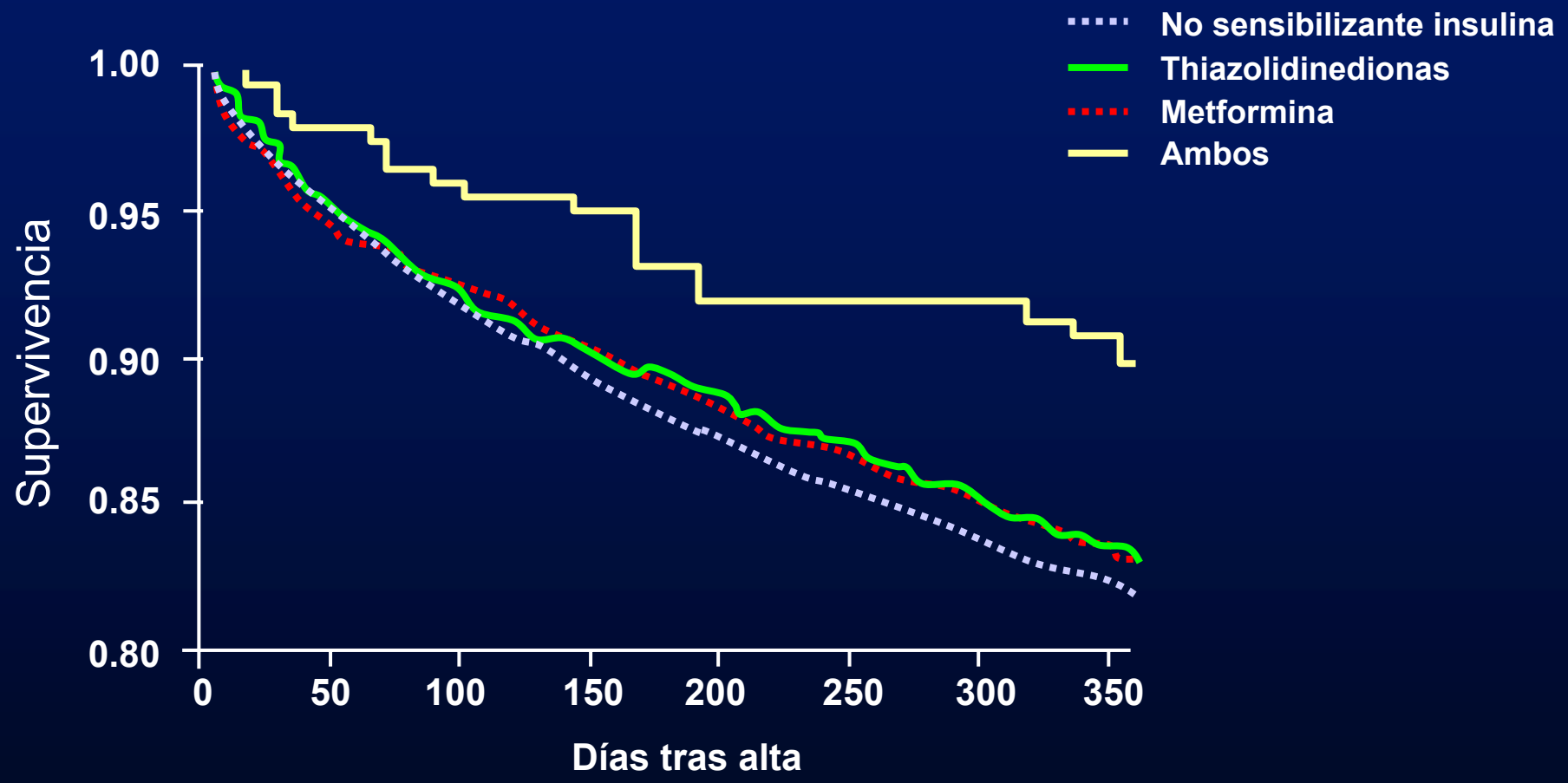
No. at Risk						
Conventional therapy	411	387	345	246	116	7
Metformin	342	328	296	239	124	11

The proportions of patients in the United Kingdom Prospective Diabetes Study who had any diabetes-related end point (Panels A and B), myocardial infarction (Panels C and D) or who died from any cause (Panels E and F) are shown for the sulfonylurea–insulin group versus the conventional-therapy group and for the metformin group versus the conventional-therapy group.

Rury R. Holman et al. N Engl J Med 2008;359

J.R.G. JUANATEY
C.H.U.Santiago

Efecto de metformina, glitazonas o ambas sobre la mortalidad después de IAM



24,953 diabéticos, seguimiento tras IAM.

SE Inzucchi et al. ***Diabetes Care 2005;*** **28:1680–1689**

Glitazonas (Rosiglitazona) y Riesgo CVC

... y Finalmente ¿Qué Hacer?

¿Qué dicen las Agencias Regulatorias?

J.R.G. JUANATEY
C.H.U.Santiago

FDA News

FDA U.S. Food and Drug Administration Department of Health and Human Services

FDA Decision Nov 14

- **At this time, FDA has concluded that there isn't enough evidence to indicate that the risks of heart attacks or death are different between Avandia and some other oral type 2 diabetes treatments. Therefore, FDA has requested that GSK conduct a new long-term study to evaluate the potential cardiovascular risk of Avandia, compared to an active control agent. GSK has agreed to conduct the study and FDA will ensure it is initiated promptly.**

http://www.fda.gov/bbs/topics/NEWS/2007/NEW01743.html

emeA. European Medicines Agency.

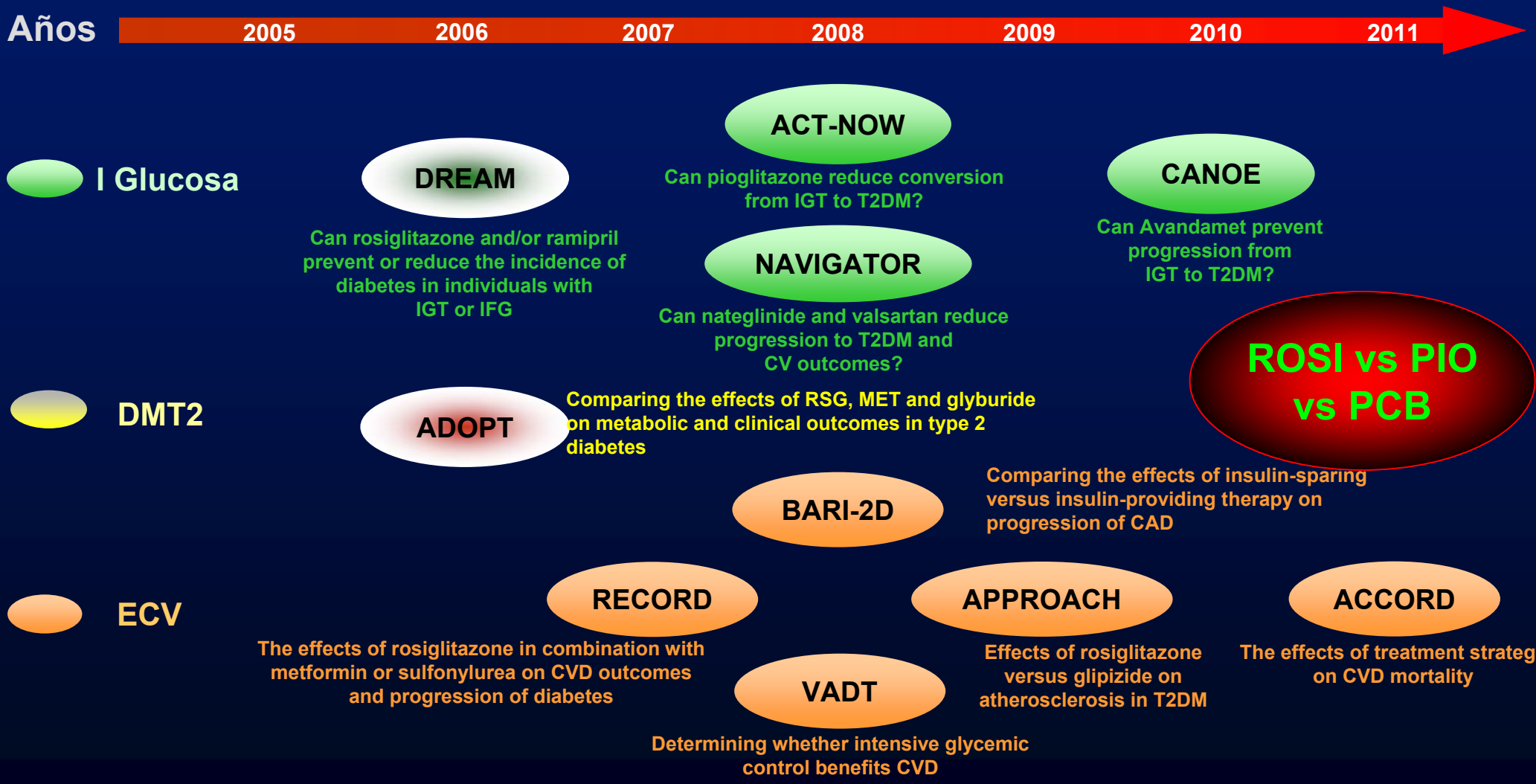
Press Office

emeA. Recomendación, 24 de Enero

Agencia Española de Medicamentos y Productos Sanitarios (28.I.2008)

1. Contraindicación para uso en pacientes con SCA.
2. Especial precaución en pacientes co cardiopatía isquémica y arteriopatía periférica sintomática.
3. En la ficha técnica se mencionará que no existen datos definitivos sobre el incremento de riesgo de cardiopatía isquémica

Ensayos Clínicos en el "Continuum Metabólico"



Gerstein HC, *et al. Diabetologia* 2004; 47:1519–1527. Viberti G, *et al. Diabetes Care* 2002; 25:1737–1743. Home PD, *et al. Diabetologia* 2005; 48:1726–1735. Sobel BE, *et al. Circulation* 2003; 108:500. Abraira C, *et al. J Diabetes Complications* 2003; 17:314–322. http://www.accordtrial.org

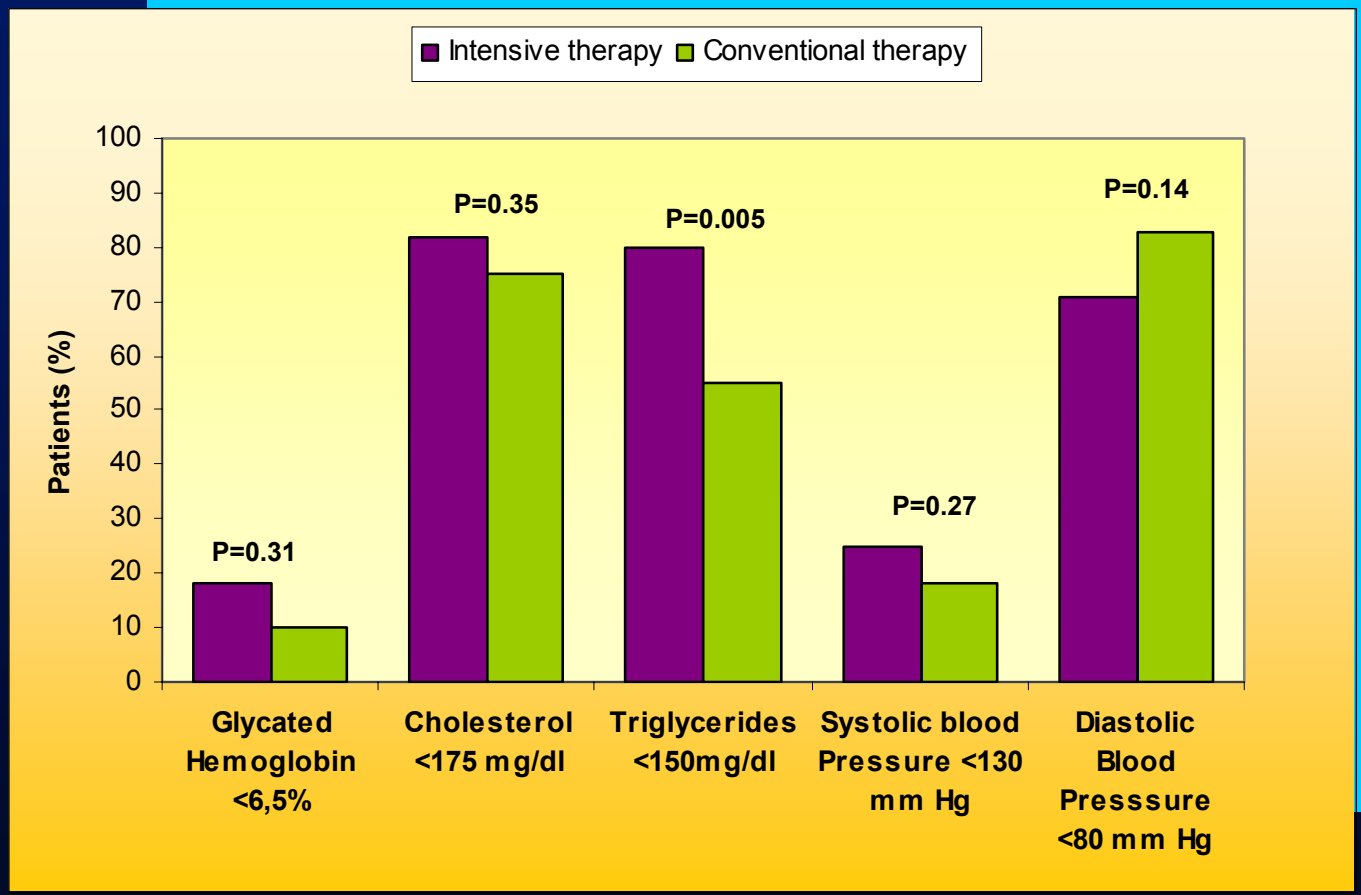
J.R.G. JUANATEY
C.H.U.Santiago

Control Glucémico en la Cardiopatía Isquémica

- Diabetes y Cardiopatía Isquémica
- Control Glucémico en Diabéticos con CI
- Fármacos antidiabéticos en Pacientes con CI
- **Prevención integral**

Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes

Changes in Selected Risk Factors during the Interventional Study and Follow-up Period

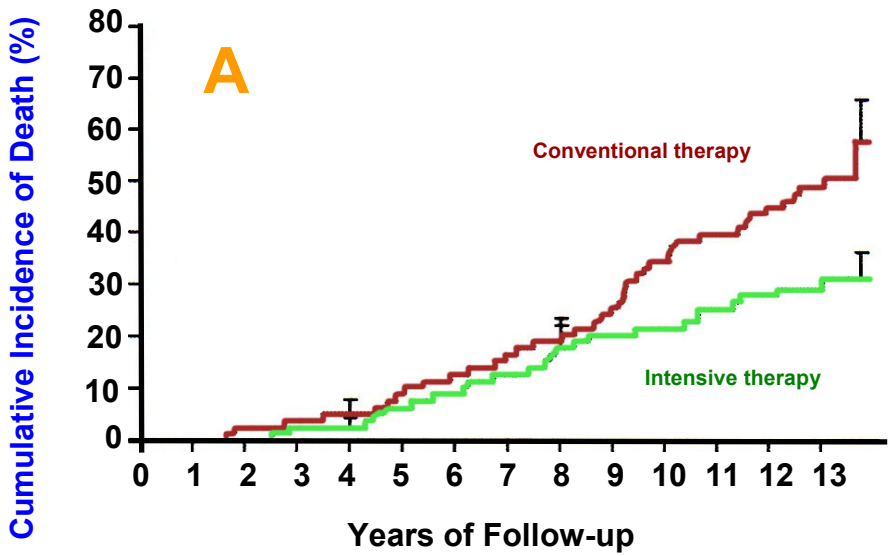


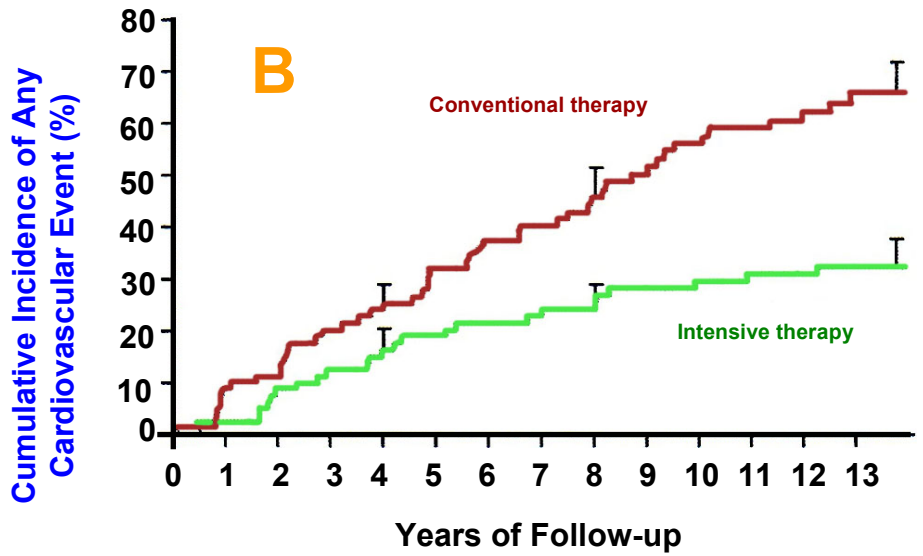
Shows the percentage of patients in each group in whom the treatment goals for the intensive-therapy group were reached at the end of the study. Only one patient (in the intensive-therapy group) reached all five treatment goals at the end of follow-up. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586. To convert the val-ues for triglycerides to millimoles per liter, multiply by 0.01129. LDL denotes low-density lipoprotein.

Gaede P et al. N Engl J Med 2008; 358:580-91.

Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes

Kaplan-Meier Estimates of the Risk of Death from Any Cause and from Cardiovascular Causes and the Number of Cardiovascular Events, According to Treatment Group





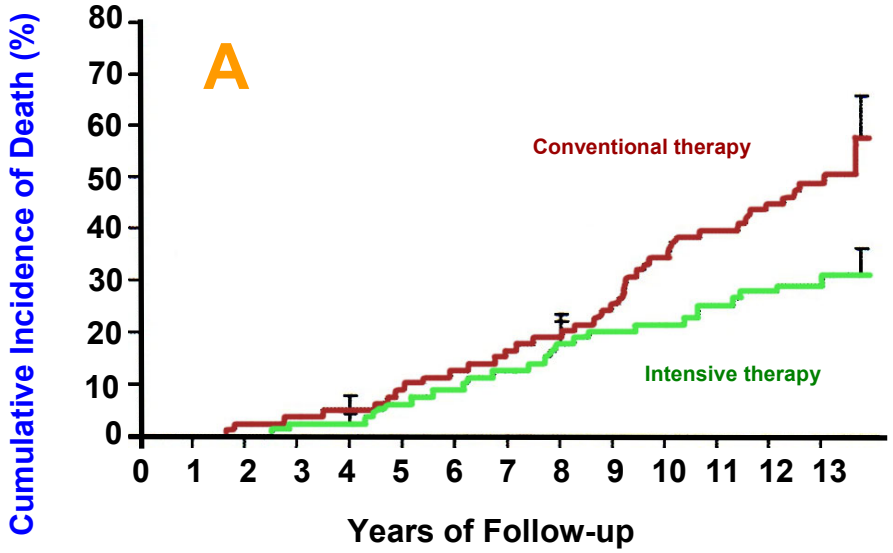
No. At Risk

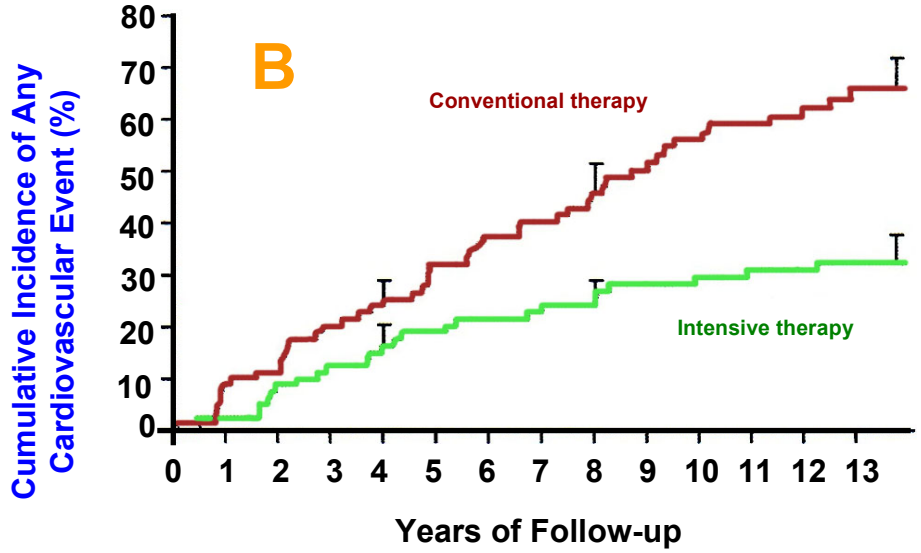
80	78	75	72	65	62	57	39	Conventional therapy	80	72	65	61	56	50	47	31
80	80	77	69	63	51	43	30	Intensive therapy	80	70	60	46	38	29	25	14

Gaede P. et al. N Engl J Med 2008; 358:580-91

Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes

Kaplan-Meier Estimates of the Risk of Death from Any Cause and from Cardiovascular Causes and the Number of Cardiovascular Events, According to Treatment Group





No. At Risk

80	78	75	72	65	62	57	39	Conventional therapy	80	72	65	61	56	50	47	31
80	80	77	69	63	51	43	30	Intensive therapy	80	70	60	46	38	29	25	14

Gaede p. et al. N Engl J Med 2008; 358:580-91

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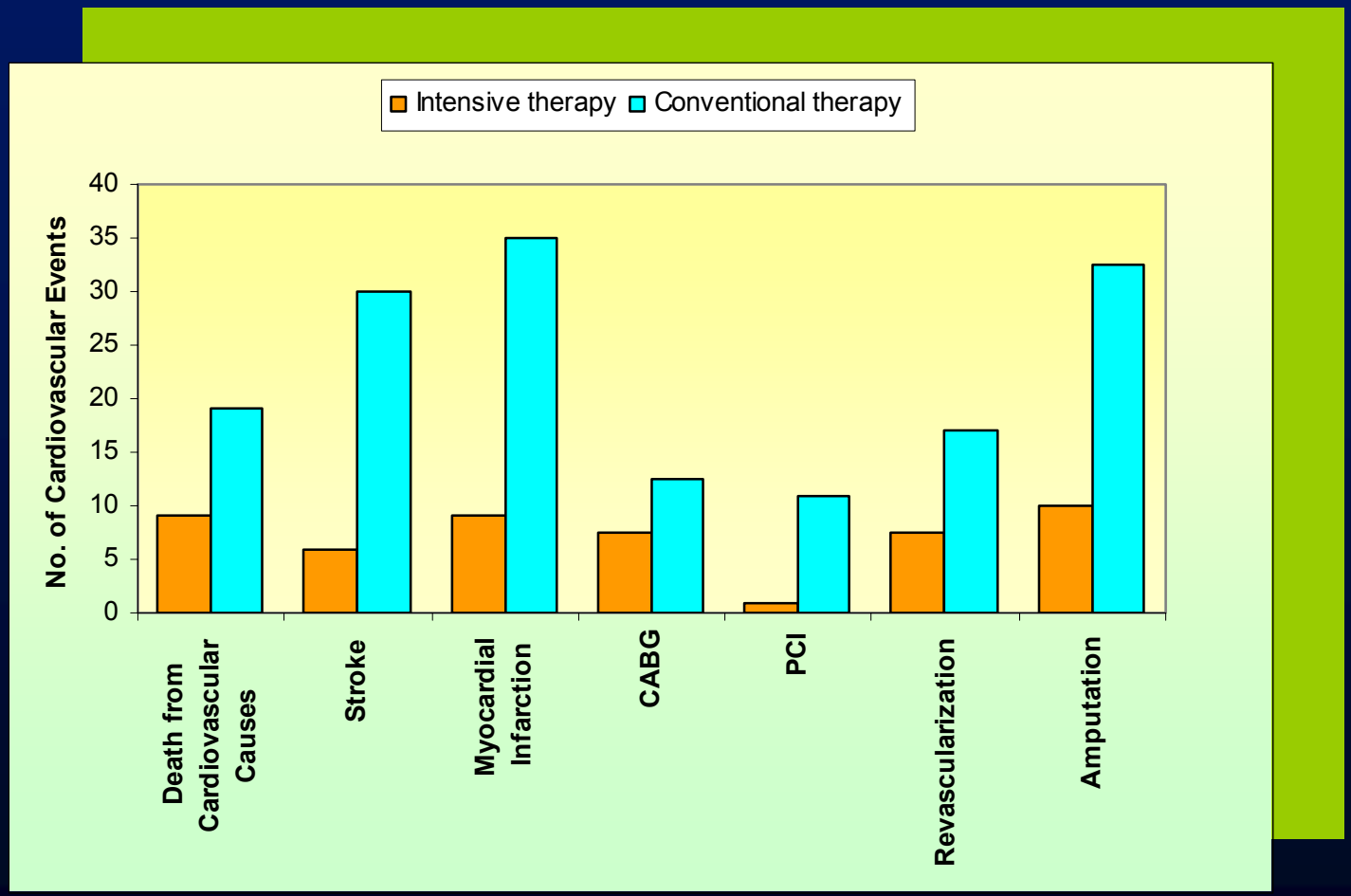
Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes

Kaplan-Meier Estimates of the Risk of Death from Any Cause and from Cardiovascular Causes and the Number of Cardiovascular Events, According to Treatment Group

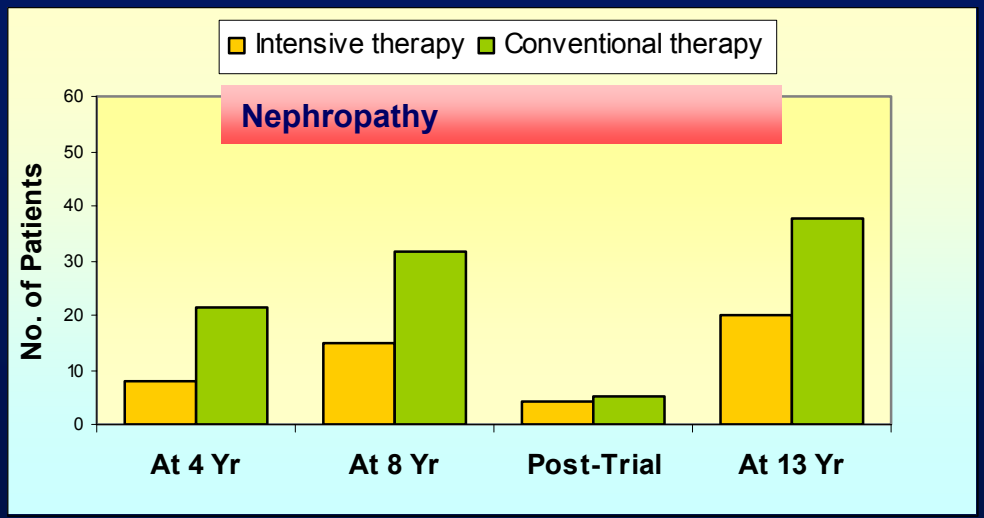


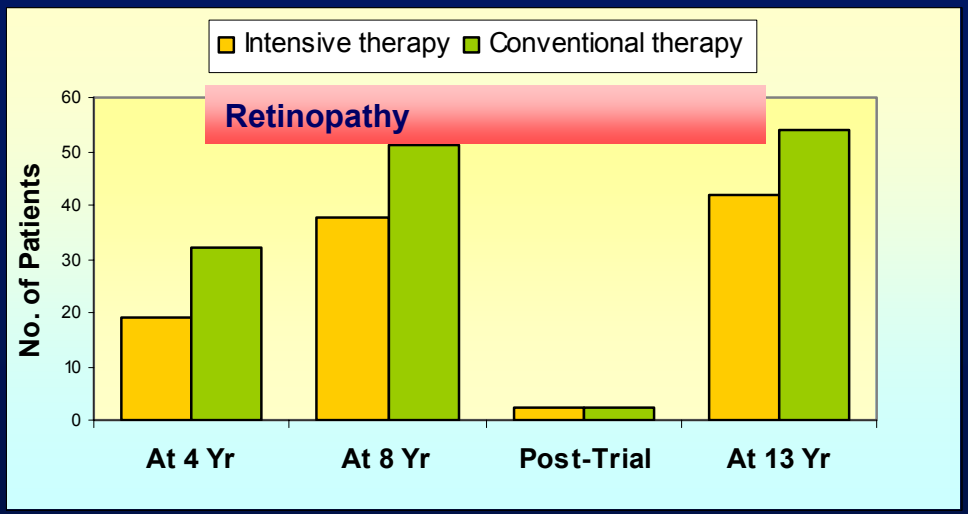
Shows the number of events for each component of the composite end point.

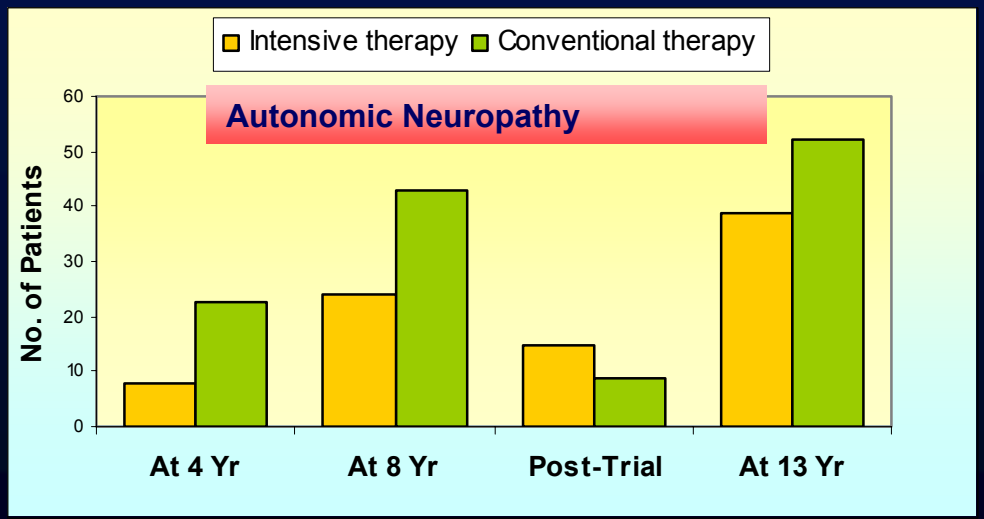
Gaede P et al. N Engl J Med 2008; 358:580-91.

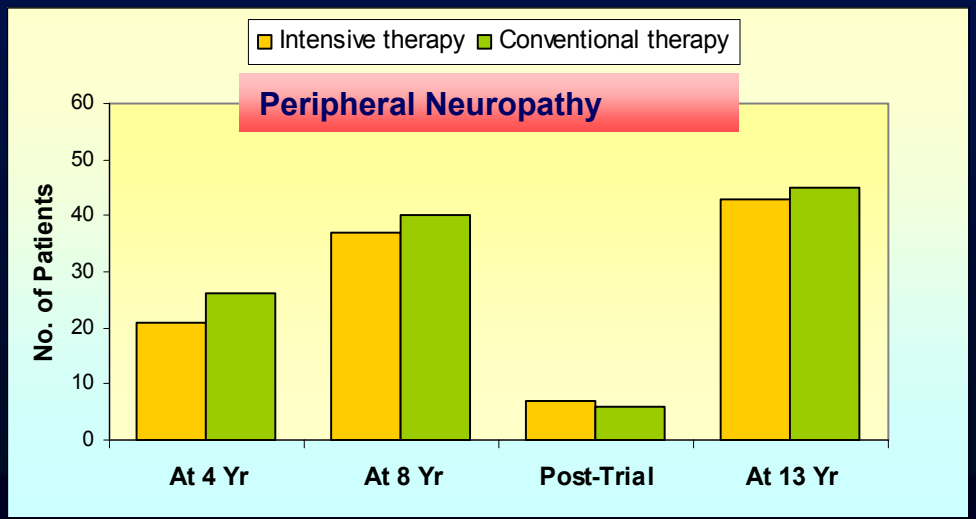
Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes

Patients with Development or Progression of Diabetic Nephropathy, Retinopathy, Autonomic Neuropathy, and Peripheral Neuropathy









Gaede P. et al. N Engl J Med 2008; 358:580-91.

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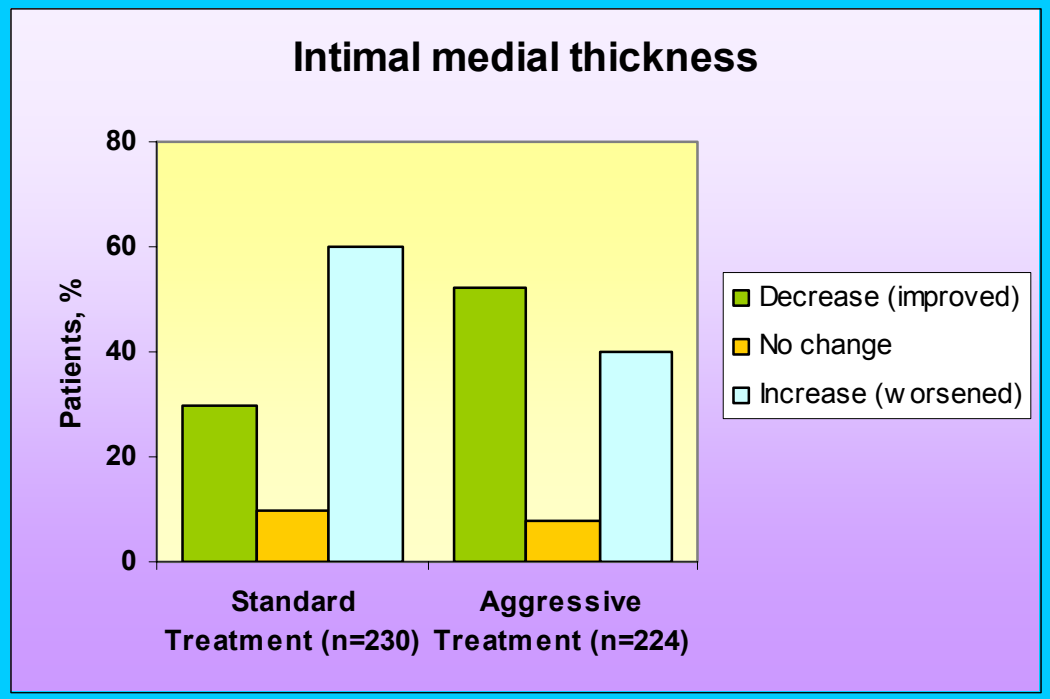
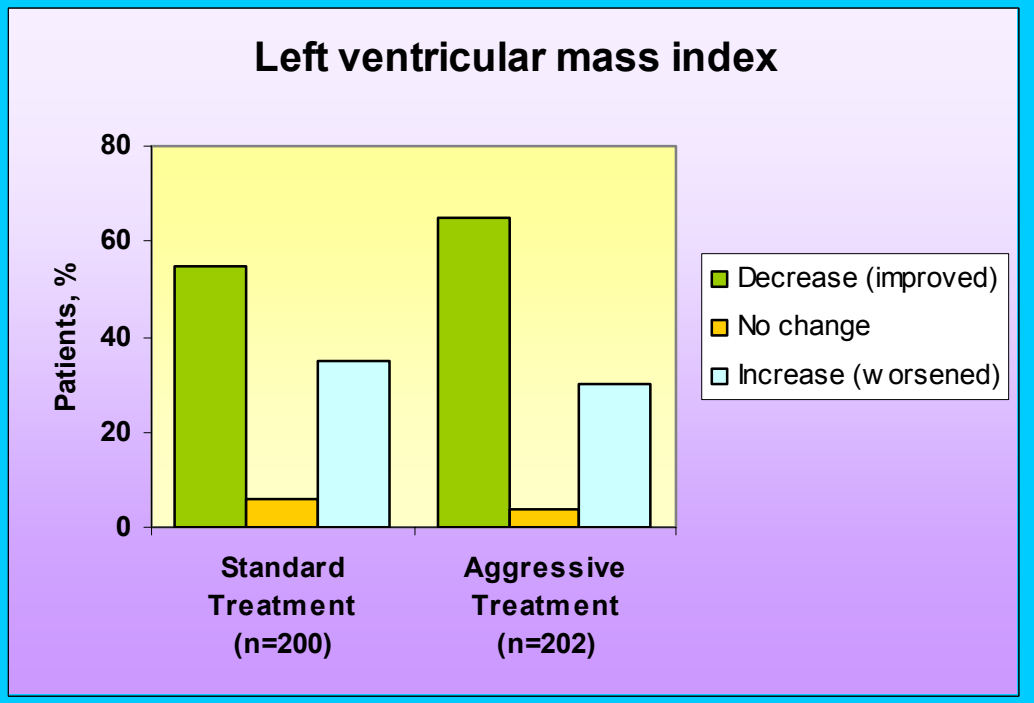
Effect of Lower Targets for Blood Pressure and LDL Cholesterol on Atherosclerosis in Diabetes

Categorical Changes in Left Ventricular Mass Index And Intimal Medial Thickness by Treatment Group





For intimal medial thickness, n=454; P value <.001. For left ventricular mass index, n=402; P value=.17. The "no change" category was defined as ±0.01 mm for intimal medial thickness or ±0.05 gm/m$^{2.7}$ for left ventricular mass index. P is for trend by each treatment group for intimal medial thickness and left ventricular mass index.

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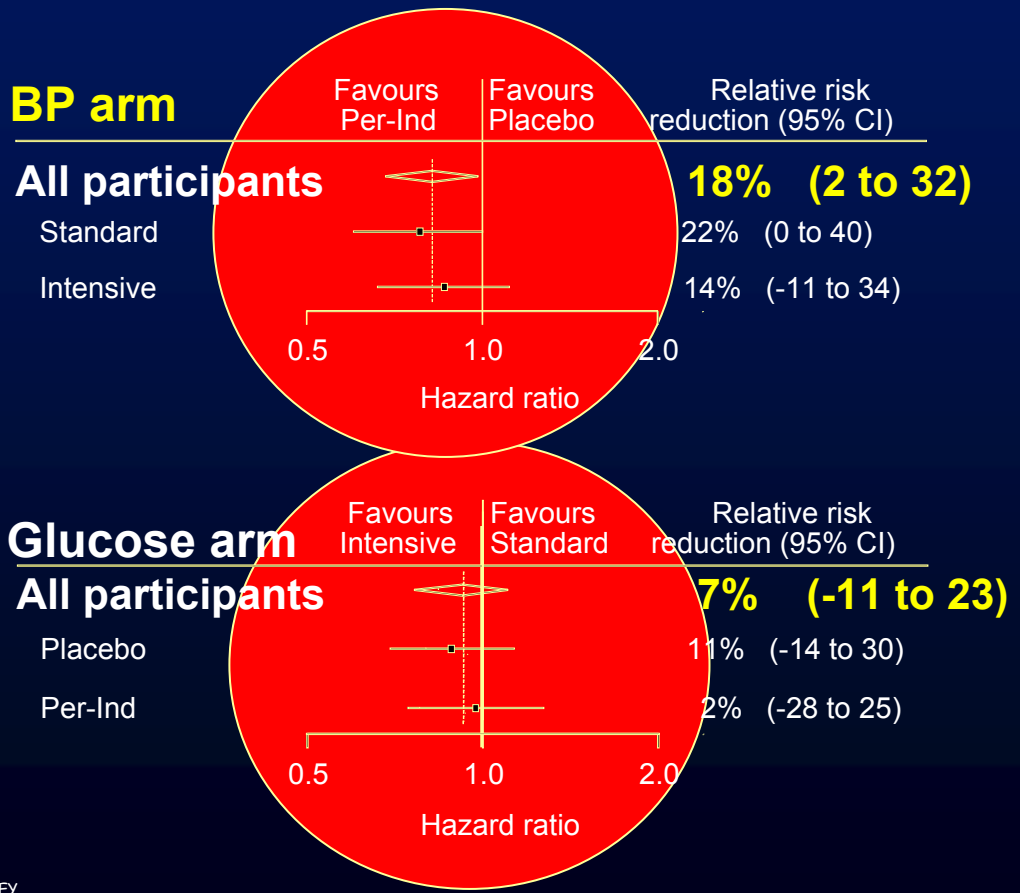
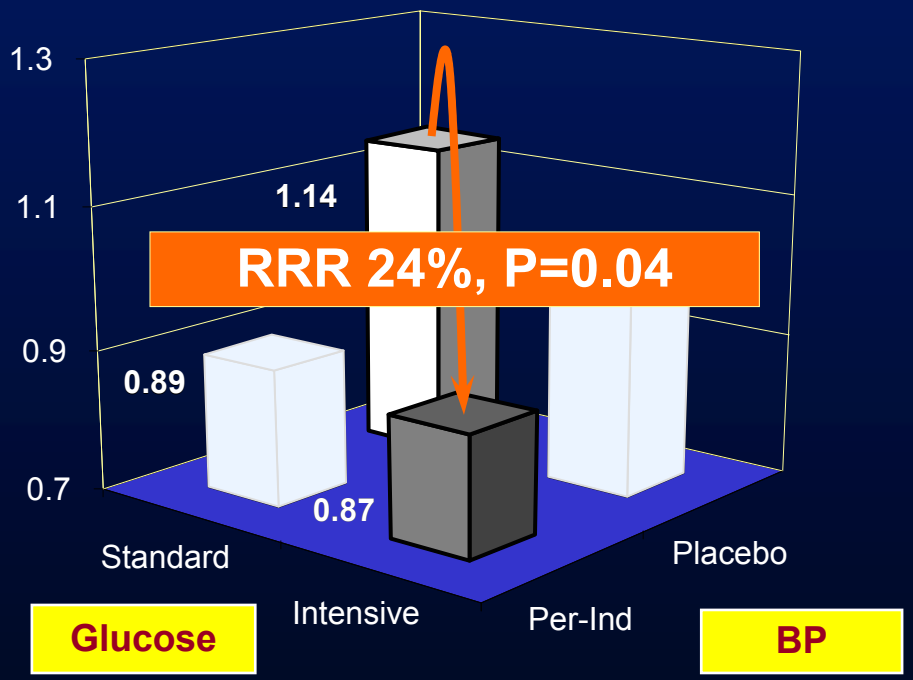
Howard BV et al. JAMA, April 9, 2008;, Vol 299 1678-1689

ADVACNCE.Cardiovascular death

Hazard ratios



Annual event rate %



P for interaction=0.62

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Terapia Antiaterosclerótica en Diabetes

Dislipemia

Estatinas
Fibratos
Tiazolidinedionas?

Modificaciones Estilo de Vida

Hipertensión

IECAs
ARA II
β-bloqueantes
Calcioantagonistas
Diuréticos

Aterosclerosis

Hiperglicemia Insulinorresistencia

Insulina
Metformina
Tiazolidinedionas
Sulfonilureas
Secretagogos
Nonsulfonilureas

Agregación y Activación Plaquetaria

Aspirina
Clopidogrel
Ticlopidina

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